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Review

Role of Plant-Derived Active Constituents in Cancer Treatment and Their Mechanisms of Action

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Abstract: Despite significant technological advancements in conventional therapies, cancer remains one of the main causes of death worldwide. Although substantial progress has been made in the control and treatment of cancer, several limitations still exist, and there is scope for further advancements. Several adverse effects are associated with modern chemotherapy that hinder cancer treatment and lead to other critical disorders. Since ancient times, plant-based medicines have been employed in clinical practice and have yielded good results with few side effects. The modern research system and advanced screening techniques for plants' bioactive constituents have enabled phytochemical discovery for the prevention and treatment of challenging diseases such as cancer. Phytochemicals such as vincristine, vinblastine, paclitaxel, curcumin, colchicine, and lycopene have shown promising anticancer effects. Discovery of more plant-derived bioactive compounds should be encouraged via the exploitation of advanced and innovative research techniques, to prevent and treat advanced-stage cancers without causing significant adverse effects. This review highlights numerous plant-derived bioactive molecules that have shown potential as anticancer agents and their probable mechanisms of action and provides an overview of in vitro, in vivo and clinical trial studies on anticancer phytochemicals.

Keywords: cancer; incidence; epidemiology; phytochemicals; mechanism; clinical trials

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1. Introduction

Cancer is a challenging disease and is the main cause of mortality worldwide; however, its impact is not evenly distributed. The cancer burden in developed and underdeveloped countries has increased over time owing to a variety of factors, including aging and growing populations, rapid socioeconomic growth, and changes in the incidence of risk factors. Owing to the growth and aging of the world population, cancer is showing reduced survival rates in many countries [1,2]. Cancer is a complex disease involving uncontrolled growth and proliferation of cells in tissues, resulting in cell aggregation locally (tumor), and it can spread to an entire organ or even to other neighboring tissues systemically (metastasis) [3]. The uncontrolled cell behavior can be caused by genetic or epigenetic changes in oncogenes involved in cell proliferation or cell death regulation [4]. The incidence and mortality rates of cancer are continuously increasing. According to a study published in 2020, the global incidence of cancer cases was 247.5, whereas the mortality rate was 127.8 per 100,000 people. Developed countries, such as Japan, Australia, New Zealand, Germany, Canada, and France, topped the list in cancer incidence and mortality rates [2]. Furthermore, breast cancer had the highest incidence rate of 11.7%, while lung cancer had the highest mortality rate of 18% [5]. The worldwide estimated incidence and mortality rates of different cancers are shown in Table 1, and the percentages of incidence and mortality of different types of cancers are shown in Figure 1.

Table 1. Estimated worldwide incidence and mortality rates (per 100,000 people) of all cancer types in 2020.

Continents	Incidence	Rank	Mortality	Rank
Worldwide	247.5	–	127.8	–
Asia	204.8	–	125.2	–
Japan	813.3	1	332.2	3
China	315.6	57	207.5	42
India	96	121	61.5	122
South Korea	449.2	42	172.8	56
Europe	587.4	–	261.1	–
Germany	750.2	4	300.9	10
France	716.9	9	284.4	17
Italy	686.8	13	289.0	15
North America	693.2	–	189.6	–
USA	689.3	12	185.0	54
Canada	726.9	7	229.7	33
South America	224.8	–	109.1	–
Brazil	278.6	63	122.3	72
Argentina	289.6	60	155.0	63
Colombia	222.5	75	108.1	81
Africa	82.7	–	53.1	–
South Africa	182.4	83	95.8	87
Morocco	160.8	93	95.5	88
Ethiopia	67.3	158	45.1	155
Australia	784.4	2	189.2	51
New Zealand	745.2	5	217.9	38

Several pathways are involved in cancer development, including the VEGF receptor pathway that can activate the RAS/RAF/MEK/ERK pathway [6] and the fibroblast growth factor (FGF) receptor pathway that activates multiple downward pathways, including the PI3K/Akt/mTOR, RAS/RAF/MEK/ERK and signal transducer and activator of transcription (STAT) pathways [7]. Reactive oxygen species (ROS) can activate the Akt/mTOR and AMPK signaling systems to induce cancer [8]. Wnt/β-catenin also plays a role in the development of multiple cancers [9]. Some important cancer-causing pathways and targets of the anticancer activity of phytochemicals are presented in Figure 2.

Since ancient times, herbal medicines have been used in health care systems. Research conducted to confirm the effectiveness of these medicines led to the discovery and development of plant-based medications. Local communities use medicinal plants to treat most diseases owing to lack of access to modern medication. In the past few decades, increasing evidence has revealed the remarkable potential plant-based therapeutics. Compared with synthetic medicines, medical plants have therapeutic potential with fewer side effects and lower costs [10].

Phytochemicals are plant-derived secondary metabolites. Based on epidemiological, in vitro, in vivo, and clinical trial data, a plant-based diet can lower the risk of many chronic diseases (e.g., neurological diseases, cardiovascular disease, diabetes, and cancer) owing to the action of bioactive plant constituents or phytochemicals [11].

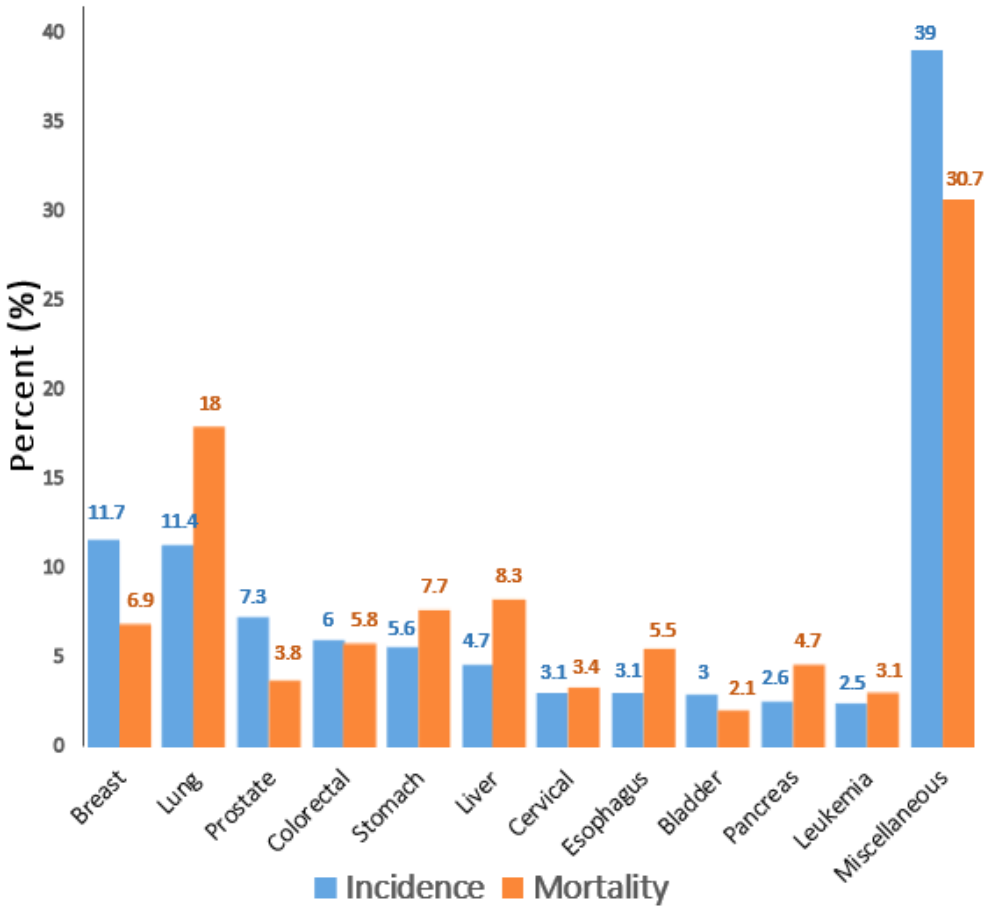

Figure 1. Incidence and mortality rates of different cancer types in 2020. Percent increases in incidence and mortality rates of different cancers are shown, with breast, lung, prostate, colorectal, and stomach cancers having the highest incidence and mortality rates. Cancers with low percent incidence and mortality rates are combined as miscellaneous cancers.

Despite significant progress in the prevention and treatment of cancer, major gaps still exist, and further improvements are warranted. Modern chemotherapy has several side effects that impede the progress of cancer treatment and lead to other serious health problems. The development of integrated research systems and advanced screening procedures for plant bioactive components has ushered in a new era of phytochemical discoveries for the prevention and treatment of complex diseases such as cancer. Bioactive compounds such as berberine, curcumin, crocetin, colchicine, gingerol, lycopene, kaempferol, resveratrol, vincristine, and vinblastine have demonstrated remarkable anticancer potential [4]. Using modern and novel research approaches, more plant-derived constituents might be discovered to prevent and treat advanced-stage cancer without significant side effects.

In this review, we highlight phytochemicals that have been reported as anticancer agents and their putative mechanisms of action in cancer treatment and summarize in vitro, in vivo, and clinical trial data on these phytoconstituents.

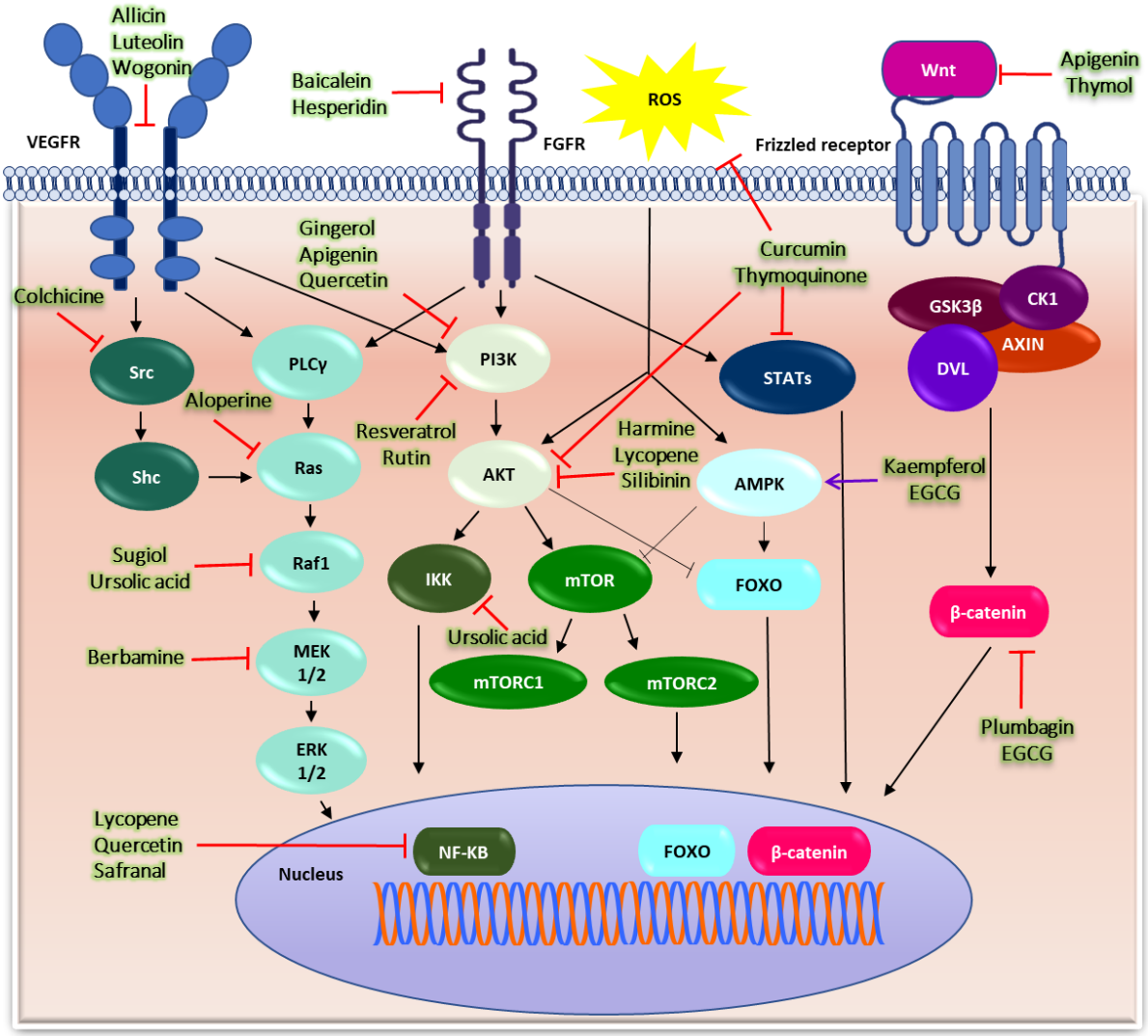

Figure 2. Important cellular mechanisms involved in cancer and mechanisms of action of phytochemical drugs. Growth factors, such as vascular endothelial growth factor and fibroblast growth factor, bind with their respective receptors, resulting in their phosphorylation, followed by the activation of downstream signaling pathways, such as the PI3K/Akt, PLCγ, and STAT pathways. Akt activates IKK, which is responsible for the activation of the NF-κB signaling and mTOR pathway; IKK exerts its effect on cells by regulating the hypoxia-induced factor. ROS activates the Akt and AMP-activated protein kinase (AMPK) pathways by inducing endoplasmic reticulum stress. AMPK activates the tumor suppressor transcription factor (FOX O) and inhibits the action of mTOR. Wnt proteins suppress glycogen synthase kinase-3β (GSK-3β) by binding to frizzled receptors, disrupting the β-catenin complex (destructive complex). β-catenin accumulates in the cytoplasm, translocates to the nucleus, and induces cell proliferation, which promotes cancer by activating Wnt-regulated genes. Different phytochemicals act on different targets to exhibit anticancer activity.

2. Methodology

Data Collection

Articles on phytoconstituents with anticancer activity were searched for using specific keywords such as "phytochemicals", "plant-derived constituents", "plant-based medicine", "antitumor", "cytotoxic", "cancer epidemiology," and "incidence" from online research databases such as PubMed, Web of Science, Medline, Google Scholar, and Science Direct and downloaded. The articles were entirely read, and data on phytochemicals with anticancer properties were collected and tabulated in Table 2.

Table 2. Plant-derived phytochemicals with potential anticancer properties, and their mechanisms of action.

Sr #	Phytochemicals	Chemical Nature	Plant's Source/Origin	Chemical Structure	M: Weight (g/mol)	Cancer Type	Study Type	Targets and Mechanisms
1	Allicin	Thioester	*Allium sativum*	$C_6H_{10O}S_2$	162.3	Lung cancer	In vitro	Downregulation of VEGF expression [12]
						Gastric cancer	In vitro	Enhanced expression of p38 and cleavage caspase-3 [13]
						Oral cancer	In vitro	Upregulation of and cleaved caspase-3 [14]
						Brain cancer	In vitro	Elevation in Fas/FasL expression [15]
2	Aloperine	Alkaloid	*Sophora alopecuroides*	$C_{15}H_{24}N_2$	232.36	Ovarian cancer	In vitro	Reactive oxygen species activation [16]
						Thyroid cancer	In vitro	Suppression of Akt pathway and downstream B-cell lymphoma (Bcl-2) expression [17]
						Prostate cancer	In vitro, in vivo	Inhibition of Akt and ERK phosphorylation [18]
						Bladder cancer	In vitro	Downregulation of Ras, p-Raf1 and p-Erk1/2 expression [19]
						Colon cancer	In vitro	Inhibition of JAK/Stat3 and PI3K/Akt pathways [20]
						Bones cancer	In vitro	Suppression of PI3K/AKT signaling [21]
3	Alpinumisoflavone	Isoflavone	*Derris eriocarpa*	$C_{20}H_{16}O_5$	336.3	Colon cancer	In vitro	Blockage of DNA repairing [22]
						Esophageal cancer	In vitro, in vivo, ex-vivo	Upregulation of miR-370 and suppression of PIM1 signaling [23]
						Brain cancer	In vitro	Suppression of glycolysis and cyclin D1 expression and activation of caspase-9 [24]
4	Amygdalin	Diglucoside	*Rosaceae kernels*	$C_{20}H_{27}NO_{11}$	457.4	Bladder cancer	In vitro	Modulation of β1 or β4 integrin expression [25]
						Breast cancer	In vitro	Downregulation of Bcl-2, upregulation of Bax and p38 MAPK signaling pathways [26]
						Prostate cancer	In vitro	Activation of caspase-3 through downregulation of Bcl-2 and up-regulation of Bax [27]
						Cervical cancer	In vitro	Downregulation of Bcl-2 and upregulation of Bax protein [28]
5	Andrographolide	Diterpenoid	*Andrographis paniculata*	$C_{20}H_{30}O_5$	350.4	Colon cancer	In vitro	Increase intracellular ROS level [29]
						Skin cancer	In vitro	Activation of JNK and p38 signaling pathway [30]
						Breast cancer	In vitro, in vivo	Suppressing of COX-2 and VEGF pathway [31]
						Prostate cancer	In vitro, in vivo	Facilitate DNA damage [32]
						Bile duct cancer	In vitro	Suppression of Claudin-1 via p-38 pathway [33]
						Ovarian cancer	In vitro	Upregulation of TIMP1 expression [34]

Table 2. *Cont.*

Sr #	Phytochemicals	Chemical Nature	Plant's Source/Origin	Chemical Structure	M: Weight (g/mol)	Cancer Type	Study Type	Targets and Mechanisms
6	Apigenin	Flavonoid	*Matricaria chamomilla*	$C_{15}H_{10}O_5$	270.24	Colon cancer	In vitro, in vivo	Inhibition of the Mcl-1, AKT, and ERK pro-survival regulators [35]
						Lung cancer	In vitro, in vivo	Inhibition of NF-κB, AKT and ERK pathway [36]
						Liver cancer	In vitro, in vivo	Inhibition of PI3K/Akt/mTOR signaling [37]
						Pancreatic cancer	In vitro	Through G2/M cell cycle arrest [38]
						Breast cancer	In vitro	Inhibition of YAP/TAZ activity [39]
						Prostate cancer	In vitro, in vivo	Suppression of NF-κB/p65 expression [40]
						Bone cancer	In vitro	Suppression of Wnt/β-catenin signaling [41]
7	Artemisinin	Alkaloid	*Artemisia annua*	$C_{15}H_{22}O_5$	282.33	Colon cancer	In vitro and in vivo	Increase in ROS production [42]
						Kidney cancer	In vitro, in vivo	Inhibition of AKT signaling [43]
						Ovarian cancer	In vitro, in vivo	Suppression of AKT/ERK/mTOR pathway [44]
						Gallbladder cancer	In vitro, in vivo	Inhibition of ERK1/2 pathway [45]
8	Baicalein	Flavonoid	*Scutellaria baicalensis*	$C_{15}H_{10}O_5$	270.24	Lung cancer	In vitro, in vivo	Suppression of VEGF, FGFR-2, and RB-1 pathways [46]
						Colon cancer	In vitro	Activation of caspase-3 [47]
						Bladder cancer	In vitro, in vivo	Inhibition of cyclin B1, MMP-2 and MMP-9 mRNA expressions [48]
						Pancreatic cancer	In vitro, in vivo	Increase caspase-3 and Bax, while decrease survivin and Bcl-2 expressions [49]
						Liver cancer	In vitro	Suppression of PI3K/Akt pathway [50]
						Prostate cancer	In vitro	Inhibition of caveolin-1/AKT/mTOR pathway [51]
						Breast cancer	In vitro, in vivo	Activation of PAX8-AS1-N activation [52]
						Ovarian cancer	In vitro, in vivo	Inhibition of YAP and RASSF6 expressions [53]
						Skin cancer	In vitro, in vivo	Inhibition of glucose uptake and metabolism of tumor cells [54]
9	Berbamine	Alkaloid	*Berberis amurensis*	$C_{37}H_{40}N_2O_6$	608.7	Blood cancer	In vitro	Upregulation of caspase-3 and downregulation of MDR-1 gene expression [55]
						Liver cancer	In vitro, in vivo, ex vivo	Inhibition of Ca2+/Calmodulin-dependent protein Kinase II expression [56]
						Ovarian cancer	In vitro, in vivo	Inhibition of Wnt/β-catenin signaling [57]

Table 2. *Cont.*

Sr #	Phytochemicals	Chemical Nature	Plant's Source/Origin	Chemical Structure	M: Weight (g/mol)	Cancer Type	Study Type	Targets and Mechanisms
						Colon cancer	In vitro	Inhibition of MEK/ERK signaling [58]
						Head & neck cancer	In vitro	Inhibition of STAT3 activation [59]
10	Capsaicin	Capsaicinoid	*Capsicum annuum*	$C18H27NO_3$	305.4	Breast cancer	In vitro, in vivo	Downregulation of FBI-1-mediated NF-κB pathway [60]
						Lung cancer	In vivo	Downregulation of MMP-2 and -9 levels [61]
						Prostate cancer	In vitro	Increases protein light chain 3-II (autophagy marker) and ROS levels [62]
						Colon cancer	In vitro	Stabilization and activation of p53 [63]
						Esophageal cancer	In vitro	Decrease hexokinase-2 (HK-2) expression [64]
						Skin cancer	In vitro	Downregulation of PI3-K/Akt/Rac1 pathway [65]
11	Cepharanthine	Alkaloid	*Stephania cepharantha*	$C_{37}H_{38}N_2O_6$	606.7	Colon cancer	In vitro	Upregulation of p21Waf1/Cip1 pathway [66]
						Breast cancer	In vitro	Inhibition of AKT/mTOR signaling [67]
						Ovarian cancer	In vitro	Increases expression of p21Waf1 and decreasing expression of cyclins A and D proteins [68]
						Liver cancer	In vitro	Activation of JNK1/2 signaling and downregulation of Akt pathway [69]
12	Chlorogenic Acid	Ester	*Etlingera elatior*	$C_{16}H_{18}O_9$	354.31	Liver cancer	In vitro, in vivo	Inhibition of DNMT1 expression [70]
						Colon cancer	In vitro	Activation of PARP-1, and caspase-9 [71]
						Breast cancer	In vitro	Upregulation of Bax and downregulation of Bcl-2 expressions [72]
13	Colchicine	Alkaloid	*Colchicum automnale*	$C_{22}H_{25}NO_6$	399.4	Gastric cancer	In vitro, in vivo	Induce caspase-3-mediated mitochondrial apoptosis [73]
						Hypopharyngeal cancer	In vitro, in vivo	Inhibition of phosphorylated FAK/SRC complex and paxillin [74]
						Breast cancer	In vitro	Inhibition of MMP-2 expression [75]
						Colon cancer	In vitro	Decrease in AKT phosphorylation [76]
14	Combretastatin A4	Stilbene	*Combretum caffrum*	$C_{18}H_{20}O_5$	316.3	Lung cancer	In vitro, in vivo	Disruption of microtubule assembly [77]
						Bladder cancer	In vitro, in vivo	Activation of caspase-3 and reduction in BubR1 and Bub3 expressions [78]
						Bone cancer	In vitro	Inhibition of NDRG1 [79]

Table 2. *Cont.*

Sr #	Phytochemicals	Chemical Nature	Plant's Source/Origin	Chemical Structure	M: Weight (g/mol)	Cancer Type	Study Type	Targets and Mechanisms
15	Corosolic acid	Tripernoid	*Lagerstroemia speciosa*	$C_{30}H_{48}O_4$	472.7	Lung cancer	In vitro, in vivo	Inhibition of VEGFR2 kinase activity [33]
						Colon cancer	In vitro, in vivo	Inhibition of HER2/HER3 receptors' heterodimerization [80]
						Gastric cancer	In vitro	Activation of AMPK pathway [81]
						Liver cancer	In vitro, in vivo, ex vivo	Inactivation of CDK19/YAP/O-GlcNAcylation pathway [82]
						Prostate cancer	In vitro, in vivo	Activation of IRE-1/JNK, PERK/CHOP and TRIB3 [83]
						Cervical cancer	In vitro	Downregulation of PI3K and Akt signaling [84]
						Kidney cancer	In vitro	Induction of lipid ROS [85]
						Breast cancer	In vitro	Increase in ROS production and decrease in VEGF concentration [86]
						Bladder cancer	In vitro, in vivo	Upregulation of SQSTM1/P62, NBR1, and UBB expression [87]
16	Crocetin	Carotenoid	*Crocus sativus*	$C_{20}H_{24}O_4$	328.4	Prostate cancer	In vitro, in vivo	Induce DNA damage and apoptosis [88]
						Colon cancer	In vitro	Upregulation FAS/FADD death receptor [89]
						Pancreatic cancer	In vitro, in vivo	Upregulation of Bax and downregulation of Bcl-2 protein [90]
						Gastric cancer	In vitro, in vivo	Upregulation of caspase-3, -8 and -9 [91]
17	Cucurbitacin	Triterpene	*Cucumis sativus*	$C_{32}H_{46}O_8$	558.7	Colon cancer	In vitro	Inhibition of Hippo-YAP Signaling Pathway [92]
						Gastric cancer	In vitro, in vivo	Suppression of Akt expression [93]
						Bile duct cancer	In vitro	Downregulation of pRB, cyclin D1 and cyclin E expression [94]
						Breast cancer	In vitro	Inhibition of Stat3 and Akt signaling [95]
18	Curcumin	Curcuminoids	*Curcuma longa*	$C_{21}H_{20}O_6$	368.38	Breast cancer	In vitro	Upregulation of PTEN/Akt signaling pathway [96]
						Gastric cancer	In vitro	Suppression of PI3K/Akt/mTOR signaling pathway [49]
						Oral cancer	In vivo	Suppression of NF-κB, and COX-2 expression [97]
						Prostate cancer	In vitro	Downregulation of NF-κB, and CXCL1 and -2 expressions [98]
						Colon cancer	In vitro	Inhibition of AMPK-induced NF-κB, uPA, and MMP9 activation [99]
						Ovarian cancer	In vitro	JAK/STAT3 pathway inhibition [100]
						Lung cancer	In vitro	Increase in FOXA2 expression [101]
19	Diosgenin	Saponin	*Dioscorea villosa*	$C_{27}H_{42}O_3$	414.6	Breast cancer	In vitro	Downregulation of Skp2 [102]
						Liver cancer	In vitro	Inhibition of Akt and upregulation of p21 and p27 expression [103]

Table 2. *Cont.*

Sr #	Phytochemicals	Chemical Nature	Plant's Source/Origin	Chemical Structure	M: Weight (g/mol)	Cancer Type	Study Type	Targets and Mechanisms
20	D-limonene	Terpene	*Citrus aurantium*	$C_{10}H_{16}$	136.23	Colon cancer	In vitro	Inactivation of Akt pathway [104]
						Lung cancer	In vitro	Upregulation of Atg5 [105]
						Prostate cancer	In vitro	Generation of ROS, and activation of caspase-3 and -9 [106]
21	Emodin	Resin	*Rheum palmatum*	$C_{15}H_{10}O_5$	270.24	Breast cancer	In vitro	Activation of AhR-CYP1A1 signaling pathway [107]
						Lung cancer	In vitro	Suppression of HAS2-HA-CD44/RHAMM pathway [108]
						Pancreatic cancer	In vitro, in vivo	Downregulation of NF-κB, VEGF, MMP-2, and -9 [109]
						Colon cancer	In vitro	Suppression of PI3K/AKT signaling [110]
						Prostate cancer	In vitro	Downregulation of VEGF [111]
22	Epigallocatechin gallate (EGCG)	Catechin	*Camellia sinensis*	$C_{22}H_{18}O_{11}$	458.4	Bile duct cancer	In vitro, in vivo	Suppression of Notch1, MMP-2, and -9 signaling [112]
						Lung cancer	In vitro	Activation of AMPK signaling pathway [113]
						Ovarian cancer	In vitro	Induce DNA damage [114]
						Prostate cancer	In vitro, in vivo	Inhibition of HSP90 function [115]
						Head & neck cancer	In vitro, in vivo	Inhibition of beta-catenin expression [116]
						Colon cancer	In vitro	Induction of ER stress through PERK/p-eIF2α/ATF4 and IRE1α pathways activation [117]
23	Erianin	Bisbenzyl	*Dendrobium chrysotoxum*	$C_{18}H_{22}O_5$	318.4	Breast cancer	In vitro	Activation PI3K/Akt pathway [118]
						Lung cancer	In vitro, in vivo	Induction of Ca2+/CaM-dependent ferroptosis [119]
						Liver cancer	In vitro, in vivo	Induction of oxidative stress-mediated mitochondrial apoptosis [73]
						Oral cancer	In vitro	Regulation of MAPK pathway [120]
						Bladder cancer	In vitro, in vivo	Increase in p-JNK level and induce c-Jun and Bcl-2 phosphorylation [121]
						Bone cancer	In vitro, in vivo	Activation of ROS/JNK signaling [122]
						Colon cancer	In vitro	Activation of JNK pathway [123]
						Cervical cancer	In vitro	Regulation of ERK1/2 signaling [124]

Table 2. *Cont.*

Sr #	Phytochemicals	Chemical Nature	Plant's Source/Origin	Chemical Structure	M: Weight (g/mol)	Cancer Type	Study Type	Targets and Mechanisms
24	Evodiamine	Alkaloid	*Evodia rutaecarpa*	$C_{19}H_{17}N_3O$	303.4	Lung cancer	In vitro, in vivo	Elevation of CD8+ T cells and downregulation of MUC1-C/PD-L1 axis [125]
						Thyroid cancer	In vitro	Through M phase cell cycle arrest and apoptosis's induction [126]
						Prostate cancer	In vitro	Activation of caspase-3 and -9 [127]
						Liver cancer	In vitro	Deactivation of PI3K/AKT pathway [128]
						Bladder cancer	In vitro	Enhance activation of P38 and JNK signaling [129]
						Colon cancer	In vitro, in vivo	Inhibition of acetyl-NF-κB, p65 and MMP-9 expression [130]
						Ovarian cancer	In vitro	Elevation of p27 and p21, and inhibition of Cdc2 expression [131]
						Pancreatic cancer	In vitro	Inhibition of NF-κB, p65, and Bcl-2 expression, while activate Bax and cleaved caspase-3 [132]
25	Flavopiridol	Flavonoids	*Dysoxylum binectariferum*	$C_{21}H_{20}ClNO_5$	41.8	Breast cancer	In vitro	Inhibition of cyclin-dependent kinases [133]
						Thyroid cancer	In vitro, in vivo	Reduction in Cyclin-dependent kinases (CDK) and MCL1 levels [134]
						Bile duct cancer	In vitro, in vivo	Suppression of cyclin-dependent kinase pathway [135]
						Head & neck cancer	In vitro, in vivo	Reduction in cyclin D1 expression [136]
						Lung cancer	In vitro	Reduction in E-cadherin level [137]
						Esophageal cancer	In vitro, in vivo	Decrease in c-Myc expression [138]
26	Gallic Acid	Phenolic acid	*Galanthus nivalis*	$C_7H_6O_5$	170.12	Lung cancer	In vitro, in vivo	Inhibition of PI3K/Akt pathway [139]
						Liver cancer	In vitro	Suppression of Wnt/β-catenin signaling [140]
						Breast cancer	In vitro, in vivo	Increases expression of cleaved caspase-7, -9, and p53, while reduces expression of Bcl-2, and PARP [141]
						Colon cancer	In vitro, in vivo	Inhibition of SRC and EGFR phosphorylation [142]
						Gastric cancer	In vitro	Increases expression of caspase-3, -8, and P53 gene [143]
						Prostate cancer	In vitro	Generation of ROS [144]
						Ovarian cancer	In vitro, in vivo	Inhibition of carbonic anhydrase IX protein [145]
						Pancreatic cancer	In vitro	Downregulation of protein Bcl-,2 while increases in BAX expression [146]

Table 2. *Cont.*

Sr #	Phytochemicals	Chemical Nature	Plant's Source/Origin	Chemical Structure	M: Weight (g/mol)	Cancer Type	Study Type	Targets and Mechanisms
27	Gambogic acid	Resin	*Garcinia hanburyi*	$C_{38}H_{44}O_8$	628.7	Lung cancer	In vitro, in vivo	Downregulation of Bcl-2, and upregulation of Bax expression [147]
						Breast cancer	In vitro, in vivo	Increase the expression of Fas, cleaved caspase-3, -8, -9 and Bax proteins [148]
						Liver cancer	In vitro	Induces apoptosis through caspases 3, -7, -8 and -9 [149]
						Prostate cancer	In vitro	Induction of ROS production [150]
						Colon cancer	In vitro, in vivo	Inhibition of Akt-mTOR signaling [151]
						Gastric cancer	In vitro, in vivo	Downregulation of circ_ASAP2 and CDK7, while upregulation of miR-33a-5p expression [152]
28	Genistein	Isoflavones	*Glycine max*	$C_{15}H_{10}O_5$	270.24	Liver cancer	In vitro	Upregulation of Bax, cleaved caspase-3 and -9 and downregulation of Bcl-2 expression [153]
						Colon cancer	In vitro, in vivo	Suppression of MiR-95, Akt and SGK1 signaling [154]
						Prostate cancer	In vitro, in vivo	Decrease MMP-2 expression [155]
						Lung cancer	In vitro	Downregulation of FoxM1 [156]
29	Gingerol	Phenol	*Zingiber officinale*	$C_{17}H_{26}O_4$	294.4	Breast cancer	In vitro	Induction of p53-dependent intrinsic apoptosis [157]
						Oral cancer	In vitro	Activate caspases and increase Apaf-1 expression [158]
						Cervical cancer		
						Lung cancer	In vitro, in vivo	Reduction in ROS and iron accumulation and suppression of USP14 expression [159]
						Pancreatic cancer	In vitro	Inhibition of PI3K/AKT signaling [160]
30	Ginkgetin	Flavonoid	*Ginkgo biloba*	$C_{32}H_{22}O_{10}$	566.5	Breast cancer	In vitro	Downregulation of estrogen receptor [161]
						Lung cancer	In vitro, in vivo	Inhibition of p62/SQSTM1 signaling [162]
						Prostate cancer	In vitro, in vivo	Suppression of STAT3 expression [163]
						Bone cancer	In vitro	Inhibition of STAT3 and activation of caspase-3/9 [164]
						Ovarian cancer	In vitro	Induction of apoptosis by activation of caspase-3 [165]
						Kidney cancer	In vitro	Suppression of JAK2-STAT3 pathway [166]
31	Glycyrrhizin	Triterpenes	*Glycyrrhiza glabra*	$C_{42}H_{62}O_{16}$	822.9	Breast cancer	In vitro, in vivo	Induces ROS-mediated apoptosis [167]
						Gastric cancer	In vitro	Downregulation of PI3K/AKT pathway [168]
						Prostate cancer	In vitro	Induces DNA damage [169]
						Ovarian cancer	In vitro	Upregulation of Fas and FasL expression [170]

Table 2. *Cont.*

Sr #	Phytochemicals	Chemical Nature	Plant's Source/Origin	Chemical Structure	M: Weight (g/mol)	Cancer Type	Study Type	Targets and Mechanisms
32	Gossypol	Phenol	*Gossypium hirsutum*	$C_{30}H_{30}O_8$	518.6	Colon cancer	In vitro	Suppression of genes coding expression for CLAUDIN1, FAS, IL2, and IL8 [171]
						Breast cancer	In vitro	Suppression of IKBKE, CCL2 and MAPK1 expression [172]
						Lung cancer	In vitro	Decrease EGFR phosphorylation and AKT/ERK signaling [173]
						Prostate cancer	In vitro	Activation of p53 protein [174]
						Ovarian cancer	In vitro	Cause changes in thiol/redox states of proteins associated with glycolysis and stress responses [175]
						Cervical cancer	In vitro, in vivo	Inhibition of FAK signaling and reversing TGF-β1-induced EMT [176]
						Head & neck cancer	In vivo	Inhibition of Bcl-X_L expression [177]
						Skin cancer	In vitro	Induces mitochondria-dependent apoptosis [178]
33	Harmine	Alkaloid	*Peganum harmala*	$C_{13}H_{12}N_2O$	212.25	Breast cancer	In vitro, in vivo	Downregulation of TAZ [179]
						Thyroid cancer	In vitro, in vivo	Downregulation of Bcl-2 and upregulation of Bax expression [180]
						Gastric cancer	In vitro	Inhibition of Akt/mTOR/p70S6K signaling [181]
						Pancreatic cancer	In vitro	Suppression of AKT/mTOR pathway [182]
						Ovarian cancer	In vitro	Inhibition of ERK/CREB pathway [183]
						Lung cancer	In vitro	Suppression of AKT phosphorylation and enhances ROS generation [184]
34	Hesperidin	Flavonoid	*Citrus limon*	$C_{28}H_{34}O_{15}$	610.6	Lung cancer	In vitro	Downregulation of FGF and NF-κB signal transduction pathways [185]
						Gastric cancer	In vitro	Increase in ROS levels and regulation of MAPK signaling [135]
						Liver cancer	In vitro	Downregulation of Bcl-xL and upregulation of Bax, Bak, and tBid proteins [186]
						Skin cancer	In vitro	Induces DNA damage [187]
						Prostate cancer	In vitro	Induces apoptosis triggered by ROS generation [188]
						Breast cancer	In vitro	Inhibition of PD-L1 expression via downregulation of Akt and NF-κB signaling [189]

Table 2. *Cont.*

Sr #	Phytochemicals	Chemical Nature	Plant's Source/Origin	Chemical Structure	M: Weight (g/mol)	Cancer Type	Study Type	Targets and Mechanisms
35	Hispidulin	Flavone	*Salvia involucrate*	$C_{16}H_{12}O_6$	300.26	Lung cancer	In vitro, in vivo	Induces ROS-mediated apoptosis via ER stress pathway [190]
						Liver cancer	In vitro, in vivo	Upregulation of PPARγ signaling [191]
						Kidney cancer	In vitro, in vivo	Activation of ROS/JNK signaling [192]
						Gastric cancer	In vitro	Activate ERK1/2 and NAG-1 signaling [193]
36	Kaempferol	Flavonoid	*Spinacia oleracea*	$C_{15}H_{10}O_6$	286.24	Breast cancer	In vitro	Increase expression of H2AX, caspase-3, and -9 [194]
						Liver cancer	In vitro	Activation of AMPK signaling [195]
						Kidney cancer	In vitro	Downregulation of AKT and FAK pathways [196]
						Cervical cancer	In vitro	Disruption of mitochondrial membrane potential and intracellular free Ca2+ concentration [197]
						Pancreatic cancer	In vitro	Inhibition of TGM2 expression [198]
						Colon cancer	In vitro	Activation of ATM and p53-Bax axis [199]
37	Kurarinone	Flavonoid	*Sophora flavescens*	$C_{26}H_{30}O_6$	438.5	Lung cancer	In vitro, in vivo	Suppression of caspase-7 and -12, and AKT pathway [200]
						Gastric cancer	In vitro	Inhibition of STAT3 signaling [201]
						Breast cancer	In vitro	Inhibition of NF-κB activation [202]
38	Lappaconitine	Diterpenoid	*Aconitum sinomontanum*	$C_{32}H_{44}N_2O_8$	584.7	Colon cancer	In vitro	Downregulation of PI3K/AKT/GSK3β signaling [203]
						Lung cancer	In vitro	Downregulation of Cyclin E1 expression [204]
						Liver cancer	In vitro	Upregulation of Bax, P53, and downregulation of Bcl-2 expressions [205]
39	Licochalcone A	Chalcone	*Glycyrrhiza glabra*	$C_{21}H_{22}O_4$	338.4	Breast cancer	In vitro	Inhibition of PI3K/Akt/mTOR pathway [206]
						Bladder cancer	In vitro	Induces ER stress-dependent apoptosis caused by activation of ER-specific caspase-12 [207]
						Lung cancer	In vitro	Induces ERK and p38 activation while suppresses JNK signaling [208]
						Liver cancer	In vitro	Downregulation of MKK4/JNK [209]
40	Liriodenine	Alkaloid	*Enicosanthellum pulchrum*	$C_{17}H_9NO_4$	275.26	Breast cancer	In vitro	Upregulation of p53 [210]
						Lung cancer	In vitro	Lockage of cell cycle progression at the G2/M phase [211]
						Ovarian cancer	In vitro	Inhibition of progression of CAOV-3 cell cycle in S phase [212]

Table 2. *Cont.*

Sr #	Phytochemicals	Chemical Nature	Plant's Source/Origin	Chemical Structure	M: Weight (g/mol)	Cancer Type	Study Type	Targets and Mechanisms
41	Luteolin	Flavonoid	*Reseda luteola*	$C_{15}H_{10}O_6$	286.24	Liver cancer	In vitro	Increases caspase-8 and decreases Bcl-2 expression [213]
						Colon cancer	In vitro	Upregulation of Nrf2 expression [214]
						Gastric cancer	In vitro	Inhibition of STAT3 phosphorylation [215]
						Oral cancer	In vitro	Suppression of EMT-induced transcription factors [216]
						Breast cancer	In vitro	Suppression of NF-κB/c-Myc activation and hTERT transcription [217]
						Pancreatic cancer	In vitro	Inhibition of VEGF expression [218]
						Lung cancer	In vitro	Inhibition of FAK-Src signaling [219]
42	Lycopene	Carotenoid	*Solanum lycopersicum*	$C_{40}H_{56}$	536.9	Breast cancer	In vitro	Inhibition of Akt phosphorylation [220]
						Prostate cancer	In vitro, in vivo	Downregulation of IL1, IL6, IL8, and TNF-α levels [221]
						Colon cancer	In vitro	Suppression of NF-κB and JNK signaling [222]
						Pancreatic cancer	In vitro	Inhibition of ROS-Mediated NF-κB Signaling [223]
						Lung cancer	In vitro, in vivo	Induction of RARβ expression [224]
						Gastric cancer	In vivo	Increase in SOD, and CAT, while decrease in MDA levels [225]
						Cervical cancer	In vitro	Upregulation of Bax, and downregulation of Bcl-2 expression [226]
						Skin cancer	In vivo	Inhibition of PCNA expression [227]
						Brain cancer	In vitro	Activation of caspase-3 pathway [228]
						Ovarian cancer	In vitro, in vivo	Decrease in integrin α5 expression and MAPK activation [229]
43	Lycorine	Alkaloid	*Crinum asiaticum*	$C_{16}H_{17}NO_4$	287.31	Breast cancer	In vitro, in vivo	Inhibition of STAT3 signaling pathway [230]
						Gastric cancer	In vitro, in vivo	Enhances FBXW7-MCL1 axis level [224]
						Prostate cancer	In vitro, in vivo	Inhibition of JAK/STAT signaling [231]
						Lung cancer	In vitro, in vivo	Inhibition of Wnt/β-catenin signaling [232]
						Liver cancer	In vitro	inhibition of ROCK1/cofilin-induced actin dynamics [233]
44	Magnolol	Lignan	*Magnolia officinalis*	$C_{18}H_{18}O_2$	266.3	Lung cancer	In vitro, in vivo	Downregulation of Akt/mTOR pathway [234]
						Gallbladder cancer	In vitro, in vivo	Increase in p53 expression [235]
						Liver cancer	In vitro	Inhibition of ERK-modulated metastatic process [236]
						Prostate cancer	In vitro	Downregulation of MMP-2 and MMP-9 expression [237]
						Esophageal cancer	In vitro	Activation of MAPK pathway [238]

Table 2. *Cont.*

Sr #	Phytochemicals	Chemical Nature	Plant's Source/Origin	Chemical Structure	M: Weight (g/mol)	Cancer Type	Study Type	Targets and Mechanisms
45	Matrine	Alkaloid	*Sophora flavescens*	$C_{15}H_{24}N_2O$	248.36	Prostate cancer	In vitro	Enhances expression of GADD45B, tumor suppresser gene or AKT/GSK3β/β-catenin [239]
						Ovarian cancer	In vitro, in vivo	Suppression of PI3K/AKT/mTOR pathway expression [240]
						Colon cancer	In vitro	Upregulation of Bax, downregulation of Bcl-2, and activation of caspase-3 and -9 [241]
						Liver cancer	In vitro, in vivo	Upregulation of miR-345-5p and downregulation of circ_0027345 and HOXD3 [242]
						Lung cancer	In vitro	Downregulation of C-C chemokine receptor type 7 (CCR7) [243]
46	Myricetin	Flavonoid	*Myrica nagi Thunb*	$C_{15}H_{10}O_8$	318.23	Thyroid cancer	In vitro	DNA damaging and inducing the release of apoptosis-inducing factor (AIF) [244]
						Bladder cancer	In vitro, in vivo	Activation of caspase-3, and inhibition of Akt and MMP-9 expression [245]
						Colon cancer	In vitro	Increases BAX/BCL2 ratio and AIF release [246]
						Prostate cancer	In vitro	Inhibition of PIM1 and disruption of PIM1/CXCR4 interaction [247]
						Breast cancer	In vitro	Enhances intracellular ROS production [248]
						Lung cancer	In vitro	Inhibition of FAK-ERK signaling pathway [249]
47	Nimbolide	Limonoid triterpene	*Azadirachta indica*	$C_{27}H_{30}O_7$	466.5	Pancreatic cancer	In vitro, in vivo	Reduction in PI3K/AKT/mTOR and ERK signaling [250]
						Colon cancer	In vitro, in vivo	Inhibition of Bcl-x, CXCR4, VEGF, and NF-κB [251]
						Bladder cancer	In vitro	Stimulation of p38 MAPK and AKT phosphorylation [252]
48	Noscapine	Alkaloid	*Papaver somniferum*	$C_{22}H_{23}NO_7$	413.4	Colon cancer	In vitro	Inhibition of PI3K/AKT/mTOR pathway [253]
						Breast cancer	In vitro	Decreases NF-κB and increases IκBα expression [254]
						Lung cancer	In vitro, in vivo	Upregulation of PARP, Bax, and repression of Bcl2 expression [255]
						Prostate cancer	In vivo	Suppression of microtubule dynamics [256]
49	Oridonin	Diterpenoid	*Rabdosia rubescens*	$C_{20}H_{28}O_6$	364.4	Colon cancer	In vitro, in vivo	Downregulation of GLUT1 and induction of autophagy [257]
						Liver cancer	In vitro, in vivo	Inhibition of Akt pathway [258]
						Ovarian cancer	In vitro	Suppression of mTOR pathway [259]
						Bladder cancer	In vitro, in vivo	Inactivation of ERK and AKT signaling pathways [260]
						Esophageal cancer	In vitro, in vivo	Suppression of AKT signaling [261]

Table 2. *Cont.*

Sr #	Phytochemicals	Chemical Nature	Plant's Source/Origin	Chemical Structure	M: Weight (g/mol)	Cancer Type	Study Type	Targets and Mechanisms
						Breast cancer	In vitro	Decrease in expression of MMPs and regulation of Integrin β1/FAK pathway [262]
						Bone cancer	In vitro, in vivo	Activation of PPAR-γ and inhibition of Nrf2 pathways [263]
50	Oxymatrine	Alkaloid	*Sophora flavescens*	$C_{15}H_{24}N_2O_2$	264.36	Cervical cancer	In vitro	Suppression of AKT/mTOR [264]
						Breast cancer	In vitro	Suppress the PI3K/Akt [265]
						Pancreatic cancer	*Ion vitro*	Downregulation of Livin and Survivin expression and upregulation of Bax/Bcl-2 ratio [266]
						Prostate cancer	In vitro, in vivo	Increase in expression of p53 and Bax, and decrease in Bcl-2 level [267]
51	Physapubescin B	Steroid	*Physalis pubescens*	$C_{30}H_{42}O_8$	530.6	Ovarian cancer	In vitro	Suppress transcriptional activity of STAT3 [268]
						Kidney cancer	In vitro, in vivo	Decreases expression of HIF-2α and activation of caspase-3 and -8 [269]
52	Pinostrobin	Flavonoid	*Boesenbergia rotunda*	$C_{16}H_{14}O_4$	270.28	Cervical cancer	In vitro	Increases expressions of TRAIL, FADD and production of ROS [270]
						Breast cancer	In vitro	Downregulation of FAK and RhoA signaling [271]
						Lung cancer	In vitro	Via promoting apoptosis [272]
						Prostate cancer	In vitro	Decrease in cyclins B expression [273]
53	Piperine	Alkaloid	*Piper nigrum*	$C_{17}H_{19}NO_3$	285.34	Colon cancer	In vitro	Suppression of Wnt/β-catenin pathway [274]
						Lung cancer	In vitro	Induces p53-mediated cell cycle arrest and apoptosis via activation of caspase-3 and -9 cascades [275]
						Breast cancer	In vitro, in vivo	Induction of cell apoptosis and cell cycle blockage [276]
						Prostate cancer	In vitro	Downregulation of cyclin A & D1 [277]
54	Piperlongumine	Alkaloid	*Piper longum*	$C_{17}H_{19}NO_5$	317.34	Lung cancer	In vitro	Inhibition of Akt phosphorylation [278]
						Prostate cancer	In vitro	Induces DNA damage [279]
						Colon cancer	In vitro	Induces DNA damage via increasing ROS production [280]
55	Plumbagin	Alkaloid	*Plumbago zeylinica*	$C_{11}H_8O_3$	188.18	Breast cancer	In vitro	Upregulation of p53 and p21 [281]
						Colon cancer	In vitro	Induction of ROS formation [282]
						Liver cancer	In vitro, in vivo	Downregulation of SIVA/mTOR signaling [283]
						Prostate cancer	In vitro, in vivo	Induction of ROS production, and activation of ER stress [284]
						Lung cancer	In vitro	Activation of caspase-9 and ROS production [285]

Table 2. *Cont.*

Sr #	Phytochemicals	Chemical Nature	Plant's Source/Origin	Chemical Structure	M: Weight (g/mol)	Cancer Type	Study Type	Targets and Mechanisms
						Esophageal cancer	In vitro, in vivo	Inhibition of STAT3-PLK1-AKT signaling [286]
						Bone cancer	In vitro	Downregulation of c-Myc expression [287]
						Cervical cancer	In vitro	Downregulation of MMP 2, 9, β-catenin and N-cadherin, while upregulation of E-cadherin signaling [288]
56	Pristimerin	Triterpenoid	*Mortonia greggii*	$C_{30}H_{40}O_4$	464.6	Colon cancer	In vitro	Decreases in AKT expression [289]
						Oral cancer	In vitro	Inhibition of MAPK/Erk1/2 and Akt signaling [290]
						Prostate cancer	In vitro	Inhibition of HIF-1α [291]
						Lung cancer	In vitro	Downregulation of integrin β1 and MMP2 expression [292]
						Pancreatic cancer	In vitro	Inhibition of Akt/NF-κB/mTOR signaling [293]
57	Pterostilbene	Stilbenoid	*Polygonum cuspidatum*	$C_{16}H_{16}O_3$	256.3	Ovarian cancer	In vitro	Decreases release of NF-κB p50, and NF-κB p65 [294]
						Lung cancer	In vitro, in vivo	Enhance ROS generation, caspase-3 activity and ER stress [295]
						Breast cancer	In vitro	Inactivate AKT and mTOR signaling pathways [296]
						Colon cancer	In vitro, in vivo	Facilitate DNA repairing mediated through Top1/Tdp1 pathway [297]
58	Puerarin	Isoflavone	*Pueraria radix*	$C_{21}H_{20}O_9$	416.4	Colon cancer	In vitro	Increase Bax expression and caspase-3 activation [298]
						Prostate cancer	In vitro	Inhibition of Keap1/Nrf2/ARE signaling pathways [299]
						Lung cancer	In vitro, in vivo	Inhibition of PI3K/Akt pathway [300]
						Liver cancer	In vitro	Modulation of MAPK signaling pathway [301]
						Brain cancer	In vitro	Suppression of p-Akt and Bcl-2, while enhancement of Bax and cleaved caspase-3 expression [302]
59	Quercetin	Flavonoid	*Allium cepa*	$C_{15}H_{10}O_7$	302.23	Thyroid cancer	In vitro	Upregulation of Pro-NAG-1/GDF15 [303]
						Breast cancer	In vitro	Inactivation of caspase-3 pathway [304]
						Liver cancer	In vitro	Inhibition of PI3K/Akt and ERK pathways [305]
						Prostate cancer	In vitro	Enhances release of tumor suppressor genes i.e., PTEN, p53 and TSC [306]
						Lung cancer	In vitro	Inhibition of NF-κB Signaling [307]
60	Resveratrol	Stilbenoid	*Polygonum cuspidatum*	$C_{14}H_{12}O_3$	228.24	Colon cancer	In vitro	Inactivates PI3K/Akt signaling [308]
						Breast cancer	In vitro	Suppression of Integrin αvβ3 expression [309]
						Ovarian cancer	In vitro	Inactivation of STAT3 signaling [310]

Table 2. *Cont.*

Sr #	Phytochemicals	Chemical Nature	Plant's Source/Origin	Chemical Structure	M: Weight (g/mol)	Cancer Type	Study Type	Targets and Mechanisms
						Pancreatic cancer	In vitro	Suppression of NAF-1 expression, induces ROS accumulation, and activation of Nrf2 signaling [311]
						Gastric cancer	In vitro	Upregulation of Bax, cleaved caspase-3 and -8 while suppression of NF-κB activation [312]
						Lung cancer	In vitro, in vivo	Decreases SIRT1-mediated NF-κB activation [313]
						Skin cancer	In vitro, in vivo	Deacetylation of SIRT1-activated NF-κB [314]
61	Rutin	Flavonoid	*Ruta graveolens*	$C_{27}H_{30}O_{16}$	610.5	Colon cancer	In vitro	Inhibition of caspase-3 expression [315]
						Brain cancer	In vitro	Upregulation of P53 expression [265]
						Skin cancer	In vitro	Suppression of PI3K/Akt and Wnt/β-catenin signaling [316]
						Breast cancer	In vitro, in vivo	Inhibition of tyrosine kinase c-Met receptor [317]
62	Safranal	Alkaloid	*Crocus sativus*	$C_{10}H_{14}O$	150.22	Colon cancer	In vitro	Suppression of PI3K/Akt/ mTOR pathway [318]
						Liver cancer	In vitro	Activation of caspases-8 and -9 [319]
						Prostate cancer	In vitro, in vivo	Downregulation of AKT and NF-κB signaling [320]
						Breast cancer	In vitro	Inhibits DNA and RNA synthesis [321]
63	Shikonin	Quinone	*Lithospermum erythrorhizon*	$C_{16}H_{16}O_5$	288.29	Lung cancer	In vitro	Downregulation of PFKFB2 expression [322]
						Colon cancer	In vitro	Reduction in peroxiredoxin V (PrxV) expression [323]
						Prostate cancer	In vitro	Induces necroptosis by decreasing caspase-8 and increasing pRIP1 and pRIP3 [324]
						Liver cancer	In vitro, in vivo	Inhibition of PKM2 expression [325]
						Ovarian cancer	In vitro	Decreases Bcl-2 expression and increases BAX, caspase-3 and -9 expression [326]
						Skin cancer	In vitro, in vivo	Inhibition of MAPK pathway-mediated induction of apoptosis [327]
						Bile duct cancer	In vitro	Inhibitions of PKM2 expression [328]
						Breast cancer	In vitro	Inhibition of epidermal growth factor receptor signaling [329]
64	Shogaol	Phenol	*Zingiber officinale*	$C_{17}H_{24}O_3$	276.4	Breast cancer	In vitro	Inhibition Akt and STAT signaling pathway [330]
						Prostate cancer	In vitro, in vivo	Inhibition of STAT3 and NF-κB signaling [331]
						Lung cancer	In vitro, in vivo	Inhibits secretion of CCL2 [332]
						Cervical cancer	In vitro	Induces apoptosis and G2/M cell cycle arrest [333]

Table 2. *Cont.*

Sr #	Phytochemicals	Chemical Nature	Plant's Source/Origin	Chemical Structure	M: Weight (g/mol)	Cancer Type	Study Type	Targets and Mechanisms
65	Silibinin	Flavonolignan	*Silybum marianum*	$C_{25}H_{22}O_{10}$	482.4	Breast cancer	In vivo	Inhibition of EGF–EGFR signaling pathway [334]
						Lung cancer	In vitro, in vivo	Activation of EGFR/LOX pathway [335]
						Ovarian cancer	In vitro, in vivo	Inhibition of ERK and Akt pathway [336]
						Prostate cancer	In vitro	Suppression of vimentin and MMP-2 expression [337]
						Skin cancer	In vivo	Via Pro-Oxidant activity [338]
						Colon cancer	In vitro	Downregulation of COX-2, VEGF, MMP-2, & -9, and CXCR-4 expression [339]
						Gastric cancer	In vitro	Inhibition of STAT3 pathway [340]
66	Silymarin	Flavonolignan	*Silybum marianum*	$C_{25}H_{22}O_{10}$	482.4	Oral cancer	In vitro, in vivo	Induction of DR5/caspase-8 apoptotic signaling [289]
						Gastric cancer	In vitro	Inhibition of p-ERK and activation of p-p38 and p-JNK pathways [341]
						Colon cancer	In vitro	Increases ATF3 transcription through activation of JNK and IκK-α [291]
						Prostate cancer	In vitro	Inhibition of cyclins (A, B1, D, E) and cyclin-dependent kinase pathway [337]
						Breast cancer	In vitro, in vivo	Regulation of MAPK signaling pathway [342]
						Liver cancer	In vivo	Reduction in ROS levels [343]
67	Solamargine	Alkaloid	*Solanum nigrum L.*	$C_{45}H_{73}NO_{15}$	868.1	Gastric cancer	In vitro, in vivo	Inhibition of Erk1/2 MAPK phosphorylation [344]
						Skin cancer	In vitro	Downregulation of hILP/XIAP [345]
						Bone cancer	In vitro	Suppression of notch pathway [346]
						Liver cancer	In vitro	Induction of apoptosis [347]
						Prostate cancer	In vitro, in vivo	Suppression of MUC1 expression [348]
68	Stachydrine	Alkaloid	*Herba Leonuri*	$C_7H_{13}NO_2$	143.18	Breast cancer	In vitro	Inhibition of Akt/ERK pathways [349]
						Prostate cancer	In vitro	Inhibits CXCR3 and CXCR4 expressions [350]
69	Sugiol	Diterpene	*Salvia prionitis*	$C_{20}H_{28}O_2$	300.4	Ovarian cancer	In vitro	Blockage of RAF/MEK/ERK signaling pathway [351]
						Prostate cancer	In vitro, in vivo	Inhibits STAT3 activity and increase ROS level [352]
						Pancreatic cancer	In vitro	Induces ROS-mediated alterations in MMP [353]
						Uterine cancer	In vitro	Increases Bax and decreases Bcl-2 expressions [354]

Table 2. *Cont.*

Sr #	Phytochemicals	Chemical Nature	Plant's Source/Origin	Chemical Structure	M: Weight (g/mol)	Cancer Type	Study Type	Targets and Mechanisms
70	Tanshinone	Terpenoids	*Salvia miltiorrhiza*	$C_{18}H_{12}O_3$	276.3	Lung cancer	In vitro, in vivo	Suppression of IL-8 through NF-κB and AP-1 Pathways [355]
						Gastric cancer	In vitro, in vivo	Downregulation of STAT3 pathway [356]
						Breast cancer	In vitro	Suppression of HIF-1α and VEGF [357]
						Ovarian cancer	In vitro, in vivo	Downregulation of Bcl-2, VEGF, COX2 and upregulation of Bax expressions [358]
						Bladder cancer	In vitro	Activation of caspases 3 and -9 [359]
						Cervical cancer	In vitro	Decrease in Bcl-2, HPV 16 and E7 protein levels, while increase in Bax and caspase-3 expressions [360]
71	Tectochrysin	Flavonoids	*Alpinia oxyphylla*	$C_{16}H_{12}O_4$	268.26	Colon cancer	In vitro	Inhibition of NF-κB signaling [361]
						Prostate cancer	In vitro	Suppression of PI3K/AKT pathway [362]
						Lung cancer	In vitro	Inhibition of STAT3 signaling [363]
72	Tetrandrine	Alkaloid	*Stephania tetrandra*	$C_{38}H_{42}N_2O_6$	622.7	Cervical cancer	In vitro, in vivo	Downregulation of MMP2 and MMP9 [364]
						Breast cancer	In vivo	Upregulation of Caspase-3, Bax, and downregulation of Bcl-2, Survivin, and PARP signaling [365]
						Gastric cancer	In vitro, in vivo	Activation of caspase-3 and -9, and upregulation of apaf-1 [366]
						Colon cancer	In vitro	Inhibition of EMT transition [367]
						Prostate cancer	In vitro	Induction of DR4 and DR5 expression, and TRAIL-mediated apoptosis [368]
						Bone cancer	In vitro, in vivo	Inhibition of PTEN/Akt, MAPK/Erk and Wnt signaling pathways [369]
73	Thymol	Phenol	*Thymus vulgaris*	$C_{10}H_{14}O$	150.22	Lung cancer	In vitro	Enhances cytoplasmic membrane permeability and cell apoptosis [370]
						Breast cancer		
						Prostate cancer		
						Colon cancer	In vitro	Suppression of Wnt/β-Catenin pathway [371]
						Gastric cancer	In vitro	Activation of Bax, PARP, and caspase-8 proteins [372]

Table 2. *Cont.*

Sr #	Phytochemicals	Chemical Nature	Plant's Source/Origin	Chemical Structure	M: Weight (g/mol)	Cancer Type	Study Type	Targets and Mechanisms
74	Thymoquinone	Quinone	*Nigella sativa*	$C_{10}H_{12}O_2$	164.2	Kidney cancer	In vitro	Inhibition of AKT phosphorylation [373]
						Breast cancer	In vitro, in vivo	Through phosphorylation of p38 via ROS generation [374]
						Bladder cancer	In vitro	Inhibition of mTOR signaling [375]
						Colon cancer	In vitro	Inhibition of STAT3, JAK2- and EGF receptor tyrosine kinase [376]
						Gastric cancer	In vitro, in vivo	Inhibition of STAT3 pathway [377]
						Liver cancer	In vitro	Inhibition of IL-8 expression, and activation of TRAIL receptors [378]
						Lung cancer	In vitro	Reduction in ERK1/2 phosphorylation [379]
						Oral cancer	In vitro	Downregulation of p38β MAPK [380]
						Pancreatic cancer	In vitro	Downregulation of mucin 4 expression [381]
75	Ursolic acid	Triterpenoids	*Oldenlandia diffusa*	$C_{30}H_{48}O_3$	456.7	Ovarian cancer	In vitro	Downregulation of PI3K/AKT pathway [382]
						Lung cancer	In vitro	Enhances apoptosis-inducing factor (AIF) and endonuclease G release [383]
						Colon cancer	In vitro, in vivo	Inhibition of IL-6-mediated STAT3 pathway [384]
						Breast cancer	In vitro	Downregulation of Nrf2 expression [385]
						Pancreatic cancer	In vitro, in vivo	Inhibition of NF-κB and STAT3 pathways [386]
						Gallbladder cancer	In vitro	Activation of caspase-3, -9 and PARP pathway [387]
76	Withaferin-A	steroidal lactone	*Withania somnifera*	$C_{28}H_{38}O_6$	470.6	Breast cancer	In vitro	Inhibition of TASK-3 expression [388]
						Oral cancer	In vitro	Upregulation of Bim and Bax expression [389]
						Skin cancer	In vitro	Activation of TRIM16 [390]
						Bone cancer	In vitro	Inactivation of Notch-1 signaling [391]
						Colon cancer	In vitro, in vivo	Inhibition of STAT3 Transcriptional activity [392]
77	Wogonin	Flavonoid	*Scutellaria baicalensis*	$C_{16}H_{12}O_5$	284.26	Colon cancer	In vitro	Increases ER stress, and mediates p53 phosphorylation [393]
						Cervical cancer	In vitro	Inhibition of Cdk4 and cyclin D1 [394]
						Lung cancer	In vitro	Downregulation of SGK1 protein levels [395]
						Bone cancer	In vitro	Increases ROS level [396]
						Breast cancer	In vitro	Activation of ERK and p38 MAPKs pathways [397]
						Ovarian cancer	In vitro	Increase in p53 and decrease in VEGF proteins expression [398]

Table 2. *Cont.*

Sr #	Phytochemicals	Chemical Nature	Plant's Source/Origin	Chemical Structure	M: Weight (g/mol)	Cancer Type	Study Type	Targets and Mechanisms
78	Xanthatin	Sesquiterpene lactone	*Xanthium strumarium*	$C_{15}H_{18}O_3$	246.3	Skin cancer	In vitro, in vivo	Inhibition of Wnt/β-catenin pathway [399]
						Lung cancer	In vitro, in vivo	Inhibition of GSK-3β signaling [400]
						Breast cancer	In vitro, in vivo	Inhibition of VEGFR2 signaling [401]
						Colon cancer	In vitro	Inhibition of mTOR pathway [402]

3. Data Analysis

A total of 78 plant-derived compounds belonging to various families were found to have significant anticancer activity; tested via in vitro and in vivo experiments. Most of these phytochemicals were alkaloids 19 (24%), flavonoids 14 (18%), terpenes 12 (15%), isoflavones 5 (6%), and phenols 5 (6%) (Figure 3).

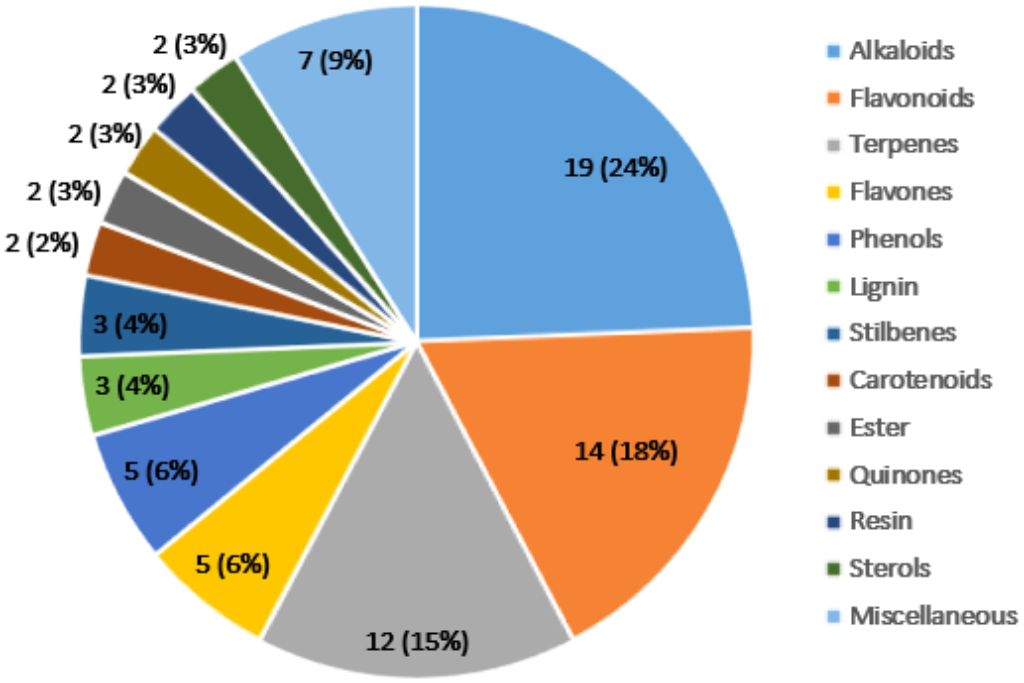

Figure 3. Numbers and percentages of anticancer phytochemicals belonging to different phytochemical classes. In this review, most phytochemicals were found to be constituted of alkaloids followed by flavonoids, terpenes, flavones, and phenols. The phytochemicals classes that have less than two phytochemicals are included in the miscellaneous class.

Multiple phytochemicals were found to exhibit activity against multiple cancers. Most of the phytochemicals were found to be effective against breast (55), lung and colon (53 each), prostate (45), liver (30), ovarian (27), gastric (24), pancreatic (18), cervical (14), bladder (13), skin (11), oral (9), kidney (7), esophageal and thyroid (6 each), bile duct and brain (5 each), and miscellaneous (10) cancers (Table 3).

Table 3. Number of effective phytochemicals against different types of cancer.

Cancer Type	Number of Phytochemicals	Cancer Type	Number of Phytochemicals	Cancer Type	Number of Phytochemicals
Breast cancer	55	Pancreatic cancer	18	Esophageal cancer	6
Colon cancer	53	Cervical cancer	14	Thyroid Cancer	6
Lung cancer	53	Bladder cancer	13	Bile duct cancer	5
Prostate cancer	45	Bladder cancer	13	Brain cancer	5
Liver cancer	30	Skin cancer	11	Miscellaneous	10
Ovarian Cancer	27	Oral cancer	9	NA	NA
Gastric cancer	24	Kidney cancer	7	NA	NA

Of the total phytochemicals, lycopene was found to exhibit activity against 10 different types of cancer; baicalin, corosolic acid, plumbagin, shikonin, and thymoquinone displayed

activity against 9; erianin, evodiamine, gallic acid, and gossypol exerted effects against 8; apigenin, curcumin, luteolin, oridonin, resveratrol, and silibinin had effects against 7; and other phytochemicals showed activity against six or less than six types of cancer (Table 4).

Table 4. Phytochemicals with activity against different number of cancer types.

Sr #	Phytochemicals	Effective against Number of Cancer Types
1	Lycopene	10
2	Baicalin, Corosolic acid, Plumbagin, Shikonin, Thymoquinone	9
3	Erianin, Evodiamine, Gallic acid, Gossypol	8
4	Apigenin, Curcumin, Luteolin, Oridonin, Resveratrol, Silibinin	7
5	Other phytochemicals	≤6

Several plant-derived active constituents, such as vincristine, vinblastine, paclitaxel, have been approved by the FDA as therapeutics for different cancers. Several other phytochemicals are currently in clinical trials for the treatment of various cancers (Table 5), and their structures are given (Figure 4).

3.1. Important Anticancer Phytochemicals from the Clinical Trials and Their Structure–Activity Relationship Data

According to a scientific report, phytochemicals may have substantial anticancer properties. Approximately 50% of the drugs approved between 1940 and 2014 were obtained directly or indirectly from natural sources [403]. Some important phytochemicals, currently in clinical trials, that showed good in vitro and in vivo potentials in different types of cancers are described below.

3.2. Curcumin

Curcumin, a lead phytochemical extracted from *Curcuma longa*, inhibits the growth of human glioma cells by inhibiting numerous cellular and nuclear factors. Curcumin increases the expression of various genes and their products, including p16, p21, and p53, Bax, EIK-1, Erk, c-Jun N-terminal kinase, early growth response protein 1, and caspases-3, -8, and -9, while reducing the expression of Bcl-2, pRB, cyclin D1, mTOR, NF-κB, and p65 [404].

The potent antioxidant property of curcumin is responsible for many of its medicinal actions, including its anticancer activity. The majority of natural antioxidative chemicals are either phenolic or -diketone compounds. But curcumin, is one of the few antioxidative compounds that has both phenolic hydroxy and -diketone groups in a single molecule [405].

In one study, researchers investigated the importance of the phenolic hydroxy groups, and other substituents in the phenyl rings of curcumin and its analogs, to their antioxidant activities by using the three antioxidant bioassays (free radical scavenging activity by the ABTS method, free radical scavenging activity by the DPPH method, and inhibition of lipid peroxidation). In all the three assays, the phenolic curcumin analogs were more potent than the non-phenolic analogs, indicating that the phenolic groups are critical for antioxidant action. Curcumin is thought to be a classic phenolic chain-breaking antioxidant, donating H atoms from phenolic groups [406,407].

Table 5. List of phytochemicals approved by the FDA or in clinical trials for various types of cancer.

Sr #	Phytochemicals	Source	Cancer Type	Development Stage	Status	Trade Name	NCT Number
1	Vincristine	*Catharanthus roseus*	Acute leukemia	FDA approved	1963	Oncovin	NA
2	Paclitaxel	*Taxus braciola*	Late-stage pancreatic cancer	FDA approved	2013	Abraxane®	NA
			Advanced non-small cell lung cancer	FDA approved	2012	Abraxane®	NA
			Metastatic breast cancer	FDA approved	2005	Abraxane®	NA
3	Curcumin	*Curcuma longa*	Prostate cancer	Phase 3	Recruiting, 15 June 2021	Biocurcumax (BCM-95) ®	NCT03769766
			Cervical cancer	Phase 2	Not yet recruiting, 25 June 2021	Curcugreen (BCM-95) ®	NCT04294836
			Pancreatic cancer	Phase 2	Recruiting, 2020	NA	NCT00094445
			Gastric cancer	Phase 2	Not yet recruiting, 13 January 2022	Meriva®	NCT02782949
			Breast cancer	Phase 1	Recruiting, 23 February 2021	NA	NCT03980509
4	Lycopene	*Solanum lycopersicum*	Prostate cancer	Phase 3	Completed, 23 January 2018	NA	NCT01105338
5	Resveratrol	*Polygonum cuspidatum*	Multiple myeloma cancer	Phase 2	Terminated (collecting more data) 27 February 2019	SRT501	NCT00920556
			Colon cancer	Phase 1	Completed, 14 June 2017	SRT501	NCT00920803
			Neuroendocrine cancer	NA	Completed, 18 November 2019	NA	NCT01476592
6	Capsaicin	*Capsicum annuum*	Breast cancer	Phase 3	Recruiting, 29 December 2021	Qutenza®	NCT03794388
			Head and neck cancer	Phase 2	Recruiting, 5 August 2021	Qutenza®	NCT04704453
			Prostate cancer	Phase 2	Not yet recruiting, 16 January 2014	Cayenne	NCT02037464

Table 5. *Cont.*

Sr #	Phytochemicals	Source	Cancer Type	Development Stage	Status	Trade Name	NCT Number
7	Chlorogenic acid	*Etlingera elatior*	Lung cancer	Phase 2	Recruiting, 26 November 2018	NA	NCT03751592
8	Colchicine	*Colchicum autumnale*	Liver cancer	Phase 2	Recruiting, 11 February 2020	Colchicine	NCT04264260
9	Genistein	*Glycine max*	Prostate cancer	Phase 2	Temporarily suspended, 4 December 2020	NA	NCT02766478
			Colorectal cancer	Phase 2	Completed, 10 May 2019	Bonistein	NCT01985763
			Prostate cancer	Phase 2	Completed, 6 August 2019	Novasoy 400	NCT01036321
			Bladder cancer	Phase 2	Completed, 10 June 2021	NA	NCT00118040
10	Camptothecin	*Camptotheca acuminata*	Solid tumor	Phase 2	Completed, 28 May 2020	CRLX101	NCT00333502
			Stomach and esophageal cancer	Phase 2	Completed, 1 February 2018	CRLX101	NCT01612546
			Advanced non-small cell lung cancer	Phase 2	Completed, 28 May 2020	CRLX101	NCT01380769
11	Piperine	*Piper nigrum*	Prostate cancer	Phase 2	Not yet recruiting, 3 November 2021	NA	NCT04731844
12	Silibinin	*Silybum marianum*	Prostate cancer	Phase 2	Completed, 31 March 2014	Silibin-Phytosome	NCT00487721
13	Quercetin	*Allium cepa*	Squamous cell carcinoma	Phase 2	Recruiting, 28 October 2021	NA	NCT03476330
14	Epigallocatechin gallate	*Camellia sinensis*	Colon cancer	Phase 1	Recruiting, 15 December 2021	Teavigo™	NCT02891538
			Esophageal cancer	Phase 1	Recruiting, 10 September 2021	NA	NCT05039983

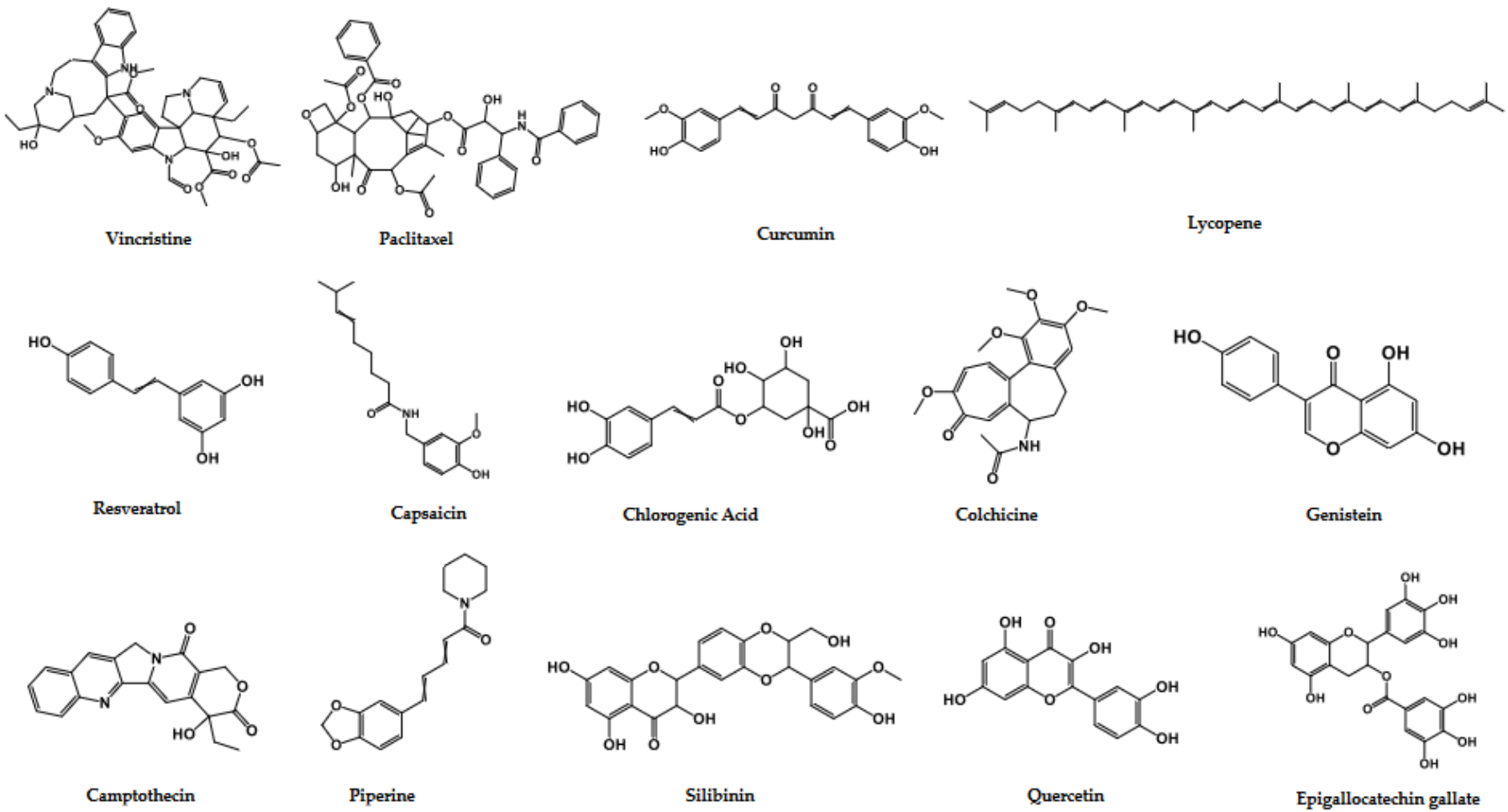

Figure 4. Structures of anticancer phytochemicals approved by FDA or in clinical trials.

In another research study, curcumin analogs were synthesized or isolated from natural sources and evaluated for AR inhibitory activity in prostate cancer cell lines. Among these analogs, few exhibited the greatest inhibitory activity against the transcription of AR, while others showed less or no activity. Based on the bioassay results, researchers showed the SAR of curcumin analogs as anti-AR reagents as follows. (1) The conjugated β-diketone moiety is required for the activity. Saturating or removing the C=C bonds resulted in a decrease or loss of activity, while converting the β-diketone moiety to pyrazole leads to a reduction or loss of activity. (2) When the methylene group in the linker was not substituted, the inhibitory activity was significantly increased by substituting the phenolic hydroxy groups with methoxy or methoxycarbonylmethoxy groups. (3) Adding an ethoxycarbonylethyl group to the central methylene group dramatically improved the anti-AR action of curcumin when the phenyl ring substitution was retained. (4) Anti-AR activity was lost in all electron-withdrawing substitutions in the phenyl rings. The exact mechanism through which curcumin analogs block AR transcription is undisclosed [408–411]. Further initiatives need to be taken to extend the SAR and enhance anti-AR activities of curcumin.

3.3. Epigallocatechin Gallate (EGCG)

EGCG is the chief constituent of green tea that can restore the expression of tumor suppressor genes such as retinoid X receptor-alpha in breast cancer, ultimately preventing breast cancer by binding to other high-affinity proteins such as Zap-70 [412]. EGCG is also found to be effective against lung, colon, and prostate cancers by inducing DNA damage and AMPK signaling and inhibiting Notch1, MMP-2/9, and β-catenin expression [115,117,331].

In EGCG structure, the three aromatic rings are connected by a pyran ring. The structure of EGCG is thought to be responsible for its health-promoting properties. The potent antioxidant effect of catechins is achieved through quinone and semiquinone synthesis, which involves oxidation of phenolic groups with atomic or single electron transfer in the periphery aromatic rings [413,414]. These rings have been linked to a decrease in proteasome activity. Protected analogues are the only ones that suppress proteasome activity. In vitro, dehydroxylation of either one or both periphery aromatic rings, inhibits proteasome inhibitory activity. Furthermore, the apoptotic cell death is induced by these protected analogues in tumor cell-specific manure. These findings showed that the periphery aromatic rings peracetate protected EGCG analogues, have a lot of potential as anti-cancer and cancer-prevention drugs [415]. The first structure–activity correlations between EGCG and heat-shock protein 90 were described and analyzed by Khandelwal et al. His findings suggest that phenolic groups on the aromatic ring, adjacent to pyrin ring, are useful in inhibiting heat-shock protein 90, whereas phenolic substituents on the faraway periphery ring are unfavorable [416]. Finally, when compared to catechins without the 5′-hydroxyl group, the hydroxyl group at the 5′-position in the upper aromatic ring inhibited urease up to 100-fold and also prevented Helicobacter pylori growth in the gut [417].

3.4. Genistein

Genistein, a potent anticancer compound, can be isolated from soybeans, lentils, chickpeas, and beans. It exhibits a pro-apoptotic effect in colon cancer and has a variety of functions: it upregulates Bax and p21, blocks topoisomerase II and NF-κB, and increases the expression of antioxidant enzymes such as glutathione peroxidase [418].

Genistein is a natural flavonoid that has been found to interact with several biological targets. After orally administration, its quick breakdown into inactive metabolites and rapid excretion from the body, are the main disadvantages of using genistein as a chemotherapeutic agent [419]. Therefore, to obtain better bioavailability compounds than genistein, a delayed compound metabolism is required. In one study, it was found that the proportion of metabolites was affected by the nature of the glycosidic bond. The metabolization of genistein derivatives with a more stable C-glycosidic bond was slower than derivatives with an O-glycosidic bond. It was also reported that linking a sugar moiety to the genistein structure increases its metabolism time in the body [420].

In another research work, it has been found that in comparison to the genistein parent molecule, novel genistein glycosyl derivatives with an O-glycosidic or C-glycosidic linkage have better antiproliferative effects. [421,422]. The C-7 or C-4′-hydroxyalkyl ethers of genistein (intermediates in the glycoconjugates synthesis), are found to be more active in preventing tumor cell growth than genistein. Furthermore, biological investigations have also revealed that derivatives with a substituent at the C-7 position inhibit the cell cycle in the G2 phase, whereas derivatives with a substituent at the C-4′ position disrupt the cell cycle in the G1 phase. [421]. It is concluded that the structural modification (hydroxyl group etherification) of genistein, successfully improved its antiproliferative activity.

3.5. Lycopene

Lycopene is a vibrant red pigment found in tomatoes, red carrots, watermelons, and red papaya. It plays a key role in targeting the PI3K/Akt pathway in stomach and pancreatic cancers by suppressing the expression of Bcl-2, an Erk protein. In breast, endometrial, prostate, and colon cancers, lycopene upregulates antioxidant enzymes GSH, GPxn, and GST and eliminates oxidative injury induced by toxins. Lycopene has been demonstrated to affect the growth and progression of HT-29 cells in culture and tumors in animal models by interfering with numerous cellular signal transduction pathways such as those of JNK and NF-κB. Lycopene also prevents infiltration, metastasis, and multiplication of human SW480 colon cancer cells by inhibiting JNK and NF-κB activation, and suppressing the production of COX-2, IL-1, IL-6, IL-10, and iNOS [423,424].

Carotenoids promoted the expression of phase II enzymes by activating the electrophile/antioxidant response element (EpRE/ARE) transcription pathway. Phase II detoxifying enzymes are a key biological method for minimizing cancer risk. By disrupting the inhibitory effect of Keap1 on Nrf2, the key EpRE/ARE activating transcription factor; certain electrophilic phytonutrients have been demonstrated to stimulate the EpRE/ARE system. However, carotenoids like lycopene are hydrophobic, lacking an electrophilic group, which is unlikely to activate Nrf2 and the EpRE/ARE system directly. The active mediators in lycopene's activation of the EpRE/ARE system are carotenoid oxidation products. Researchers discovered the main structure–activity rules for EpRE/ARE activation using a series of described mono- and di-apocarotenoids that might potentially be produced from in vivo metabolism of carotenoids (lycopene). Such as active molecules are the aldehydes, not acids; the methyl group on the terminal aldehyde, which regulates the reactivity of the conjugated double bond, is responsible for the activity, and the main chain of the molecule is constituted of the dialdehyde's optimum length (12 carbons). The apocarotenals suppressed breast and prostate cancer cell proliferation with an efficacy comparable to that of EpRE/ARE activation. These findings may provide a molecular explanation for the cancer-preventive properties of carotenoids like lycopene [425,426].

3.6. Resveratrol

Resveratrol, a naturally occurring polyphenol, is found in peanuts, mulberries, grapes, blueberries, and bilberries. It plays a significant role in the treatment of different types of cancers, including colorectal, breast, pancreatic, liver, lung, and prostate cancers, by increasing the expression of Bax and p53 and decreasing the expression of NF-κB, AP-1, Bcl-2, MMPs, cyclins, COX-2, cyclin-dependent kinases, and cytokines. Resveratrol has been recognized to impede angiogenesis and suppress VEGF by decreasing MAP kinase phosphorylation [418].

A research study was carried out to find the structure–activity relationship of resveratrol in cancer. It was observed that the number and position of free phenolic hydroxyl groups have a key role in the anticancer activities of resveratrol. For this purpose, the researchers used different analogs of resveratrol having different phenolic hydroxyl groups for their anticancer activities in T24 cells. They found that the oxyresveratrol (3-OH glycosylated RV, having an extra -OH group than RV) has greater inhibitory effect that RV but polydatin (3-OH glycosylated RV, lack of one -OH group) has a lesser effect than RV.

This showed that the increased number of phenolic hydroxyl groups are responsible for the anticancer activity of RV [427]. Herath et al. proved the theory by discovering that when the hydroxyl groups in RV were replaced, the drug's pharmacological activity decreased [428]. Furthermore, Miksits et al. found that all of RV's sulfated metabolites were less effective against various cancer cell lines [309]. This suggests that the anti-tumor efficacy of RV can be affected by the conjugation of phenolic hydroxyl groups with sulfuric acid. Hence, again it is proved that the free phenolic hydroxyl groups are important for antitumor effect of RV.

Currently, several investigations on plant-based drugs to treat cancer are ongoing. Some well-known and effective phytochemicals, such as vincristine, were approved by the FDA in 1963 to treat acute leukemia (brand name, Oncovin). Furthermore, paclitaxel was approved for the treatment of metastatic breast cancer, advanced lung cancer, and pancreatic cancer in 2005, 2012, and 2013, respectively, under the brand name, Abraxane. Curcumin, lycopene, and capsaicin, which are under phase-III trials for prostate and breast cancers, are promising candidates for cancer therapy. Quercetin, genistein, silibinin, and EGCG are undergoing clinical trials or treatment for various types of cancers.

This study of anticancer plant-derived phytochemicals will help ethnomedicine and ethnopharmacology investigations, resulting in better outcomes for the medical potential of natural resources. Various phytochemicals highlighted in this review could be further investigated in clinical trials, enabling the availability of more effective anticancer medicines with fewer adverse effects. This study will be beneficial to researchers working on or interested in the discovery of plant-based medicines for treatment of various cancers.

4. Conclusions

Researchers have found multiple synthetic drugs for the treatment of cancer, but anticancer drugs are costly and have some major adverse effects like anemia, vital organs damage, and hair and nail loss. Keeping in mind these drawbacks, we searched multiple papers on natural anticancer compounds, their mechanisms, clinicals trials and SAR data of important phytochemicals. The epidemiology data showed that the breast and lung cancers have the highest mortality and prevalence rates. In this study, we found that majority of anticancer compounds belong to alkaloids and flavonoids classes, and the highest number of phytochemicals were found to be effective against breast and lung cancers, which give us a chance to try these phytochemicals in clinical trials and discover some plant-based drugs that control these high spreading cancers. To discover effective anticancer treatments with less side effects and less cost, the world must rely upon, and conduct more research on natural resources, especially plants and their active constituents.

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Abbreviations

AIF	Apoptosis-inducing factor
Apaf-1	Apoptotic protease activating factor 1
ATF4	Activating transcription factor 4
Bcl-X_L	B-cell lymphoma-extra large
CCL2	Chemokine (C-C motif) ligand 2
CDK	Cyclin-dependent kinases
CHOP	C/EBP homologous protein
CREB	cAMP-response element binding protein
CXCR4	C-X-C chemokine receptor type 4
DR5	Death receptor 5
ER	Endoplasmic reticulum
FAK	Focal adhesion kinase
FOXA2	Forkhead box protein A2
GADD45B	Growth arrest and DNA-damage-inducible, beta protein
GLUT1	Glucose transporter 1
H2AX	H2A histone family member X
HIF-2α	Hypoxia inducible factor 2 alpha
HMGB1	High mobility group box 1 protein
HOXD3	Homeobox D3
HSP90	Heat shock protein 90
hTERT	Human telomerase reverse transcriptase
iNOS	Inducible nitric oxide synthase
IκBα	IkappaB alpha
IκK-α	Inhibitory-κB kinase alpha
JNK	Jun N-terminal kinase
Keap1	Kelch-like ECH-associated protein 1
LOX	Lysyl oxidase
MEK	MAPK/ERK kinase
mTOR	Mammalian target of rapamycin
MUC1-C	Mucin 1, cell surface associated protein
NAF-1	Nuclear assembly factor 1
NAG-1	NSAID activated gene 1
NBR1	Neighbor of BRCA1 gene 1
Nrf2	Nuclear factor erythroid 2–related factor 2
PD-L1	Programmed death-ligand 1
PKM2	Pyruvate kinase M2
PLK1	Polo-like kinase 1
PPARγ	Peroxisome proliferator- activated receptor gamma
PTEN	Phosphatase and tensin homolog deleted in chromosome 10
Raf	Rapidly accelerated aibrosarcoma
RASSF6	Ras-association domain family
RHAMM	HMMR hyaluronan-mediated motility receptor
RhoA	Ras-homolog family member A
RIP1	Receptor interacting protein 1
ROCK1	Rho-associated protein kinase 1
ROS	Reactive oxygen species
SGK1	Serum/glucocorticoid regulated kinase 1
Skp2	S-phase kinase associated protein 2
TASK-3	Two-pore-domain acid sensitive K channel 3 TASK-3
TGF-β1	Transforming growth factor-beta1
TNF-α	Tumor necrosis factor alpha
Top1	Topoisomerase 1
TRAIL	TNF-related apoptosis-inducing ligand
TRIM16	Tripartite motif-containing protein 16
uPA	Urokinase-type plasminogen activator
USP14	Ubiquitin specific peptidase 14
Wnt	Wingless-related integration site
XIAP	X-linked inhibitor of apoptosis protein

References

1. World Health Organization. *International Agency for Research on Cancer*; World Health Organization: Geneva, Switzerland, 2019.
2. Cao, W.; Chen, H.-D.; Yu, Y.-W.; Li, N.; Chen, W.-Q. Changing profiles of cancer burden worldwide and in China: A secondary analysis of the global cancer statistics 2020. *Chin. Med. J.* **2021**, *134*, 783. [CrossRef] [PubMed]
3. Martin, T.A.; Ye, L.; Sanders, A.J.; Lane, J.; Jiang, W.G. Cancer invasion and metastasis: Molecular and cellular perspective. In *Madame Curie Bioscience Database [Internet]*; Landes Bioscience: Austin, TX, USA, 2013.
4. Garcia-Oliveira, P.; Otero, P.; Pereira, A.G.; Chamorro, F.; Carpena, M.; Echave, J.; Fraga-Corral, M.; Simal-Gandara, J.; Prieto, M.A. Status and challenges of plant-anticancer compounds in cancer treatment. *Pharmaceuticals* **2021**, *14*, 157. [CrossRef] [PubMed]
5. Sung, H.; Ferlay, J.; Siegel, R.L.; Laversanne, M.; Soerjomataram, I.; Jemal, A.; Bray, F. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J. Clin.* **2021**, *71*, 209–249. [CrossRef] [PubMed]
6. Li, L.; Zhao, G.D.; Shi, Z.; Qi, L.L.; Zhou, L.Y.; Fu, Z.X. The Ras/Raf/MEK/ERK signaling pathway and its role in the occurrence and development of HCC. *Oncol. Lett.* **2016**, *12*, 3045–3050. [CrossRef]
7. Farooq, M.; Khan, A.W.; Kim, M.S.; Choi, S. The Role of Fibroblast Growth Factor (FGF) Signaling in Tissue Repair and Regeneration. *Cells* **2021**, *10*, 3242. [CrossRef]
8. Zhao, Y.; Hu, X.; Liu, Y.; Dong, S.; Wen, Z.; He, W.; Zhang, S.; Huang, Q.; Shi, M. ROS signaling under metabolic stress: Cross-talk between AMPK and AKT pathway. *Mol. Cancer* **2017**, *16*, 1–12. [CrossRef]
9. Zhang, Y.; Wang, X. Targeting the Wnt/β-catenin signaling pathway in cancer. *J. Hematol. Oncol.* **2020**, *13*, 1–16. [CrossRef]
10. Khan, A.W.; Khan, A.U.; Shah, S.M.M.; Ullah, A.; Faheem, M.; Saleem, M. An updated list of neuromedicinal plants of Pakistan, their uses, and phytochemistry. *Evid. Based Complement. Alternat. Med.* **2019**, *2019*, 6191505. [CrossRef]
11. Catalano, E. Role of phytochemicals in the chemoprevention of tumors. *arXiv* **2016**, arXiv:1605.04519.
12. Alhasan, L.; Addai, Z.R. Allicin-induced modulation of angiogenesis in lung cancer cells (A549). *Trop. J. Pharm. Res.* **2018**, *17*, 2129–2134. [CrossRef]

13. Zhang, X.; Zhu, Y.; Duan, W.; Feng, C.; He, X. Allicin induces apoptosis of the MGC-803 human gastric carcinoma cell line through the p38 mitogen-activated protein kinase/caspase-3 signaling pathway. *Mol. Med. Rep.* **2015**, *11*, 2755–2760. [CrossRef] [PubMed]
14. Guo, Y.; Liu, H.; Chen, Y.; Yan, W. The effect of allicin on cell proliferation and apoptosis compared to blank control and cis-platinum in oral tongue squamous cell carcinoma. *Onco Targets Ther.* **2020**, *13*, 13183. [CrossRef] [PubMed]
15. Li, C.; Jing, H.; Ma, G.; Liang, P. Allicin induces apoptosis through activation of both intrinsic and extrinsic pathways in glioma cells. *Mol. Med. Rep.* **2018**, *17*, 5976–5981. [CrossRef] [PubMed]
16. Qiu, M.; Liu, J.; Su, Y.; Liu, J.; Wu, C.; Zhao, B. Aloperine induces apoptosis by a reactive oxygen species activation mechanism in human ovarian cancer cells. *Protein Pept. Lett.* **2020**, *27*, 860–869. [CrossRef] [PubMed]
17. Lee, Y.-R.; Chen, S.-H.; Lin, C.-Y.; Chao, W.-Y.; Lim, Y.-P.; Yu, H.-I.; Lu, C.-H. In vitro antitumor activity of aloperine on human thyroid cancer cells through caspase-dependent apoptosis. *Int. J. Mol. Sci.* **2018**, *19*, 312. [CrossRef] [PubMed]
18. Ling, Z.; Guan, H.; You, Z.; Wang, C.; Hu, L.; Zhang, L.; Wang, Y.; Chen, S.; Xu, B.; Chen, M. Aloperine executes antitumor effects through the induction of apoptosis and cell cycle arrest in prostate cancer In Vitro and In Vivo. *Onco Targets Ther.* **2018**, *11*, 2735. [CrossRef]
19. Zhang, L.; Liang, J.; Liu, X.; Wu, J.; Tan, D.; Hu, W. Aloperine exerts antitumor effects on bladder cancer In Vitro. *Onco Targets Ther.* **2020**, *13*, 10351. [CrossRef]
20. Zhang, L.; Zheng, Y.; Deng, H.; Liang, L.; Peng, J. Aloperine induces G2/M phase cell cycle arrest and apoptosis in HCT116 human colon cancer cells. *Int. J. Mol. Med.* **2014**, *33*, 1613–1620. [CrossRef]
21. Chen, S.; Jin, Z.; Dai, L.; Wu, H.; Wang, J.; Wang, L.; Zhou, Z.; Yang, L.; Gao, W. Aloperine induces apoptosis and inhibits invasion in MG-63 and U2OS human osteosarcoma cells. *Biomed. Pharmacother.* **2018**, *97*, 45–52. [CrossRef]
22. Li, D.; Li, X.; Li, G.; Meng, Y.; Jin, Y.; Shang, S.; Li, Y. Alpinumisoflavone causes DNA damage in colorectal cancer cells via blocking DNA repair mediated by RAD51. *Life Sci.* **2019**, *216*, 259–270. [CrossRef]
23. Han, Y.; Yang, X.; Zhao, N.; Peng, J.; Gao, H.; Qiu, X. Alpinumisoflavone induces apoptosis in esophageal squamous cell carcinoma by modulating miR-370/PIM1 signaling. *Am. J. Cancer Res.* **2016**, *6*, 2755. [PubMed]
24. Zhao, X.; Zhang, T.; Jiang, K.; Gao, H. Alpinumisoflavone exhibits anticancer activities in glioblastoma multiforme by suppressing glycolysis (Retraction of Vol 11, Pg 631, 2019). *Anat. Rec. (Hoboken)* **2020**, *303*, 2192–2201. [CrossRef] [PubMed]
25. Makarević, J.; Rutz, J.; Juengel, E.; Kaulfuss, S.; Tsaur, I.; Nelson, K.; Pfitzenmaier, J.; Haferkamp, A.; Blaheta, R.A. Amygdalin influences bladder cancer cell adhesion and invasion In Vitro. *PLoS ONE* **2014**, *9*, e110244. [CrossRef]
26. Lee, H.M.; Moon, A. Amygdalin regulates apoptosis and adhesion in Hs578T triple-negative breast cancer cells. *Biomol. Ther.* **2016**, *24*, 62. [CrossRef] [PubMed]
27. Chang, H.-K.; Shin, M.-S.; Yang, H.-Y.; Lee, J.-W.; Kim, Y.-S.; Lee, M.-H.; Kim, J.; Kim, K.-H.; Kim, C.-J. Amygdalin induces apoptosis through regulation of Bax and Bcl-2 expressions in human DU145 and LNCaP prostate cancer cells. *Biol. Pharm. Bull.* **2006**, *29*, 1597–1602. [CrossRef] [PubMed]
28. Chen, Y.; Ma, J.; Wang, F.; Hu, J.; Cui, A.; Wei, C.; Yang, Q.; Li, F. Amygdalin induces apoptosis in human cervical cancer cell line HeLa cells. *Immunopharmacol. Immunotoxicol.* **2013**, *35*, 43–51. [CrossRef]
29. Khan, I.; Khan, F.; Farooqui, A.; Ansari, I.A. Andrographolide exhibits anticancer potential against human colon cancer cells by inducing cell cycle arrest and programmed cell death via augmentation of intracellular reactive oxygen species level. *Nutr. Cancer* **2018**, *70*, 787–803. [CrossRef]
30. Liu, G.; Chu, H. Andrographolide inhibits proliferation and induces cell cycle arrest and apoptosis in human melanoma cells. *Oncol. Lett.* **2018**, *15*, 5301–5305. [CrossRef]
31. Peng, Y.; Wang, Y.; Tang, N.; Sun, D.; Lan, Y.; Yu, Z.; Zhao, X.; Feng, L.; Zhang, B.; Jin, L. Andrographolide inhibits breast cancer through suppressing COX-2 expression and angiogenesis via inactivation of p300 signaling and VEGF pathway. *J. Exp. Clin. Cancer Res.* **2018**, *37*, 1–14. [CrossRef]
32. Forestier-Román, I.S.; López-Rivas, A.; Sánchez-Vázquez, M.M.; Rohena-Rivera, K.; Nieves-Burgos, G.; Ortiz-Zuazaga, H.; Torres-Ramos, C.A.; Martínez-Ferrer, M. Andrographolide induces DNA damage in prostate cancer cells. *Oncotarget* **2019**, *10*, 1085. [CrossRef]
33. Pearngam, P.; Kumkate, S.; Okada, S.; Janvilisri, T. Andrographolide inhibits cholangiocarcinoma cell migration by down-regulation of claudin-1 via the p-38 signaling pathway. *Front. Pharmacol.* **2019**, *10*, 827. [CrossRef] [PubMed]
34. Beesetti, S.L.; Jayadev, M.; Subhashini, G.V.; Mansour, L.; Alwasel, S.; Harrath, A.H. Andrographolide as a therapeutic agent against breast and ovarian cancers. *Open Life Sci.* **2019**, *14*, 462–469. [CrossRef] [PubMed]
35. Shao, H.; Jing, K.; Mahmoud, E.; Huang, H.; Fang, X.; Yu, C. Apigenin sensitizes colon cancer cells to antitumor activity of ABT-263. *Mol. Cancer Ther.* **2013**, *12*, 2640–2650. [CrossRef] [PubMed]
36. Chen, M.; Wang, X.; Zha, D.; Cai, F.; Zhang, W.; He, Y.; Huang, Q.; Zhuang, H.; Hua, Z.-C. Apigenin potentiates TRAIL therapy of non-small cell lung cancer via upregulating DR4/DR5 expression in a p53-dependent manner. *Sci. Rep.* **2016**, *6*, 1–17. [CrossRef]
37. Yang, J.; Pi, C.; Wang, G. Inhibition of PI3K/Akt/mTOR pathway by apigenin induces apoptosis and autophagy in hepatocellular carcinoma cells. *Biomed. Pharmacother.* **2018**, *103*, 699–707. [CrossRef]
38. Ujiki, M.B.; Ding, X.-Z.; Salabat, M.R.; Bentrem, D.J.; Golkar, L.; Milam, B.; Talamonti, M.S.; Bell, R.H.; Iwamura, T.; Adrian, T.E. Apigenin inhibits pancreatic cancer cell proliferation through G2/M cell cycle arrest. *Mol. Cancer* **2006**, *5*, 1–8. [CrossRef]
39. Li, Y.-W.; Xu, J.; Zhu, G.-Y.; Huang, Z.-J.; Lu, Y.; Li, X.-Q.; Wang, N.; Zhang, F.-X. Apigenin suppresses the stem cell-like properties of triple-negative breast cancer cells by inhibiting YAP/TAZ activity. *Cell Death Discov.* **2018**, *4*, 1–9. [CrossRef]

40. Gupta, S.; Afaq, F.; Mukhtar, H. Involvement of nuclear factor-kappa B, Bax and Bcl-2 in induction of cell cycle arrest and apoptosis by apigenin in human prostate carcinoma cells. *Oncogene* **2002**, *21*, 3727–3738. [CrossRef]
41. Liu, X.; Li, L.; Lv, L.; Chen, D.; Shen, L.; Xie, Z. Apigenin inhibits the proliferation and invasion of osteosarcoma cells by suppressing the Wnt/β-catenin signaling pathway. *Oncol. Rep.* **2015**, *34*, 1035–1041. [CrossRef]
42. Wang, J.; Zhang, J.; Shi, Y.; Xu, C.; Zhang, C.; Wong, Y.K.; Lee, Y.M.; Krishna, S.; He, Y.; Lim, T.K. Mechanistic investigation of the specific anticancer property of artemisinin and its combination with aminolevulinic acid for enhanced anticolorectal cancer activity. *ACS Cent. Sci.* **2017**, *3*, 743–750. [CrossRef]
43. Yu, C.; Sun, P.; Zhou, Y.; Shen, B.; Zhou, M.; Wu, L.; Kong, M. Inhibition of AKT enhances the anti-cancer effects of Artemisinin in clear cell renal cell carcinoma. *Biomed. Pharmacother.* **2019**, *118*, 109383. [CrossRef] [PubMed]
44. Li, X.; Zhou, Y.; Liu, Y.; Zhang, X.; Chen, T.; Chen, K.; Ba, Q.; Li, J.; Liu, H.; Wang, H. Preclinical efficacy and safety assessment of artemisinin-chemotherapeutic agent conjugates for ovarian cancer. *EBioMedicine* **2016**, *14*, 44–54. [CrossRef] [PubMed]
45. Jia, J.; Qin, Y.; Zhang, L.; Guo, C.; Wang, Y.; Yue, X.; Qian, J. Artemisinin inhibits gallbladder cancer cell lines through triggering cell cycle arrest and apoptosis. *Mol. Med. Rep.* **2016**, *13*, 4461–4468. [CrossRef] [PubMed]
46. Cathcart, M.-C.; Useckaite, Z.; Drakeford, C.; Semik, V.; Lysaght, J.; Gately, K.; O'Byrne, K.J.; Pidgeon, G.P. Anti-cancer effects of baicalein in non-small cell lung cancer in-vitro and in-vivo. *BMC Cancer* **2016**, *16*, 1–13. [CrossRef] [PubMed]
47. Palko-Labuz, A.; Sroda-Pomianek, K.; Uryga, A.; Kostrzewa-Suslow, E.; Michalak, K. Anticancer activity of baicalein and luteolin studied in colorectal adenocarcinoma LoVo cells and in drug-resistant LoVo/Dx cells. *Biomed. Pharmacother.* **2017**, *88*, 232–241. [CrossRef] [PubMed]
48. Wu, J.-Y.; Tsai, K.-W.; Li, Y.-Z.; Chang, Y.-S.; Lai, Y.-C.; Laio, Y.-H.; Wu, J.-D.; Liu, Y.-W. Anti-bladder-tumor effect of baicalein from Scutellaria baicalensis Georgi and its application In Vivo. *Evid. Based Complement. Alternat. Med.* **2013**, 2013. [CrossRef]
49. Tian, Y.; Zhen, L.; Bai, J.a.; Mei, Y.; Li, Z.; Lin, A.; Li, X. Anticancer effects of Baicalein in pancreatic Neuroendocrine tumors In Vitro and In Vivo. *Pancreas* **2017**, *46*, 1076. [CrossRef]
50. Bie, B.; Sun, J.; Li, J.; Guo, Y.; Jiang, W.; Huang, C.; Yang, J.; Li, Z. Baicalein, a natural anti-cancer compound, alters microRNA expression profiles in Bel-7402 human hepatocellular carcinoma cells. *Cell. Physiol. Biochem.* **2017**, *41*, 1519–1531. [CrossRef]
51. Guo, Z.; Hu, X.; Xing, Z.; Xing, R.; Lv, R.; Cheng, X.; Su, J.; Zhou, Z.; Xu, Z.; Nilsson, S. Baicalein inhibits prostate cancer cell growth and metastasis via the caveolin-1/AKT/mTOR pathway. *Mol. Cell. Biochem.* **2015**, *406*, 111–119. [CrossRef]
52. Yu, X.; Cao, Y.; Tang, L.; Yang, Y.; Chen, F.; Xia, J. Baicalein inhibits breast cancer growth via activating a novel isoform of the long noncoding RNA PAX8-AS1-N. *J. Cell. Biochem.* **2018**, *119*, 6842–6856. [CrossRef]
53. Li, Y.; Wang, D.; Liu, J.; Li, Y.; Chen, D.; Zhou, L.; Lang, T.; Zhou, Q. Baicalin Attenuates YAP Activity to Suppress Ovarian Cancer Stemness. *Onco Targets Ther.* **2020**, *13*, 7151. [CrossRef] [PubMed]
54. Huang, L.; Peng, B.; Nayak, Y.; Wang, C.; Si, F.; Liu, X.; Dou, J.; Xu, H.; Peng, G. Baicalein and baicalin promote melanoma apoptosis and senescence via metabolic inhibition. *Front. Cell Dev. Biol.* **2020**, *8*, 836. [CrossRef] [PubMed]
55. Dong, Q.; Zheng, S.; Xu, R.; Lu, Q.; He, L. Study on effect of berbamine on multidrug resistance leukemia K562/Adr cells. *Chin. J. Integr. Med.* **2004**, *24*, 820–822.
56. Meng, Z.; Li, T.; Ma, X.; Wang, X.; Van Ness, C.; Gan, Y.; Zhou, H.; Tang, J.; Lou, G.; Wang, Y. Berbamine inhibits the growth of liver cancer cells and cancer-initiating cells by targeting Ca2+/calmodulin-dependent protein kinase II. *Mol. Cancer Ther.* **2013**, *12*, 2067–2077. [CrossRef]
57. Zhang, H.; Jiao, Y.; Shi, C.; Song, X.; Chang, Y.; Ren, Y.; Shi, X. Berbamine suppresses cell proliferation and promotes apoptosis in ovarian cancer partially via the inhibition of Wnt/β-catenin signaling. *Acta Biochim. Biophys. Sin.* **2018**, *50*, 532–539. [CrossRef]
58. Mou, L.; Liang, B.; Liu, G.; Jiang, J.; Liu, J.; Zhou, B.; Huang, J.; Zang, N.; Liao, Y.; Ye, L. Berbamine exerts anticancer effects on human colon cancer cells via induction of autophagy and apoptosis, inhibition of cell migration and MEK/ERK signalling pathway. *J. BUON* **2019**, *24*, 1870–1875.
59. Zhu, H.; Ruan, S.; Jia, F.; Chu, J.; Zhu, Y.; Huang, Y.; Liu, G. In vitro and In Vivo superior radiosensitizing effect of berbamine for head and neck squamous cell carcinoma. *Onco Targets Ther.* **2018**, *11*, 8117. [CrossRef]
60. Chen, M.; Xiao, C.; Jiang, W.; Yang, W.; Qin, Q.; Tan, Q.; Lian, B.; Liang, Z.; Wei, C. Capsaicin Inhibits Proliferation and Induces Apoptosis in Breast Cancer by Down-Regulating FBI-1-Mediated NF-κB Pathway. *Drug Des. Devel. Ther.* **2021**, *15*, 125. [CrossRef]
61. Anandakumar, P.; Kamaraj, S.; Jagan, S.; Ramakrishnan, G.; Asokkumar, S.; Naveenkumar, C.; Raghunandhakumar, S.; Vanitha, M.K.; Devaki, T. The anticancer role of capsaicin in experimentallyinduced lung carcinogenesis. *J. Pharmacopunct.* **2015**, *18*, 19. [CrossRef]
62. Ramos-Torres, Á.; Bort, A.; Morell, C.; Rodríguez-Henche, N.; Díaz-Laviada, I. The pepper's natural ingredient capsaicin induces autophagy blockage in prostate cancer cells. *Oncotarget* **2016**, *7*, 1569. [CrossRef]
63. Jin, J.; Lin, G.; Huang, H.; Xu, D.; Yu, H.; Ma, X.; Zhu, L.; Ma, D.; Jiang, H. Capsaicin mediates cell cycle arrest and apoptosis in human colon cancer cells via stabilizing and activating p53. *Int. J. Biol. Sci.* **2014**, *10*, 285. [CrossRef] [PubMed]
64. Mao, X.; Zhu, H.; Luo, D.; Ye, L.; Yin, H.; Zhang, J.; Zhang, Y.; Zhang, Y. Capsaicin inhibits glycolysis in esophageal squamous cell carcinoma by regulating hexokinase-2 expression. *Mol. Med. Rep.* **2018**, *17*, 6116–6121. [CrossRef] [PubMed]
65. Shin, D.-H.; Kim, O.-H.; Jun, H.-S.; Kang, M.-K. Inhibitory effect of capsaicin on B16-F10 melanoma cell migration via the phosphatidylinositol 3-kinase/Akt/Rac1 signal pathway. *Exp. Mol. Med.* **2008**, *40*, 486–494. [CrossRef] [PubMed]

66. Rattanawong, A.; Payon, V.; Limpanasittikul, W.; Boonkrai, C.; Mutirangura, A.; Wonganan, P. Cepharanthine exhibits a potent anticancer activity in p53-mutated colorectal cancer cells through upregulation of p21Waf1/Cip1. *Oncol. Rep.* **2018**, *39*, 227–238. [CrossRef]
67. Gao, S.; Li, X.; Ding, X.; Qi, W.; Yang, Q. Cepharanthine induces autophagy, apoptosis and cell cycle arrest in breast cancer cells. *Cell. Physiol. Biochem.* **2017**, *41*, 1633–1648. [CrossRef]
68. Payon, V.; Kongsaden, C.; Ketchart, W.; Mutirangura, A.; Wonganan, P. Mechanism of cepharanthine cytotoxicity in human ovarian cancer cells. *Planta Med.* **2019**, *85*, 41–47. [CrossRef]
69. Biswas, K.K.; Tancharon, S.; Sarker, K.P.; Kawahara, K.I.; Hashiguchi, T.; Maruyama, I. Cepharanthine triggers apoptosis in a human hepatocellular carcinoma cell line (HuH-7) through the activation of JNK1/2 and the downregulation of Akt. *FEBS Lett.* **2006**, *580*, 703–710. [CrossRef]
70. Liu, Y.; Feng, Y.; Li, Y.; Hu, Y.; Zhang, Q.; Huang, Y.; Shi, K.; Ran, C.; Hou, J.; Zhou, G. Chlorogenic acid decreases malignant characteristics of hepatocellular carcinoma cells by inhibiting DNMT1 expression. *Front. Pharmacol.* **2020**, *11*, 867. [CrossRef]
71. Gouthamchandra, K.; Sudeep, H.; Venkatesh, B.; Prasad, K.S. Chlorogenic acid complex (CGA7), standardized extract from green coffee beans exerts anticancer effects against cultured human colon cancer HCT-116 cells. *Food Sci. Hum. Wellness.* **2017**, *6*, 147–153. [CrossRef]
72. Changizi, Z.; Moslehi, A.; Rohani, A.H.; Eidi, A. Chlorogenic acid inhibits growth of 4T1 breast cancer cells through involvement in Bax/Bcl2 pathway. *J. Cancer Res. Ther.* **2020**, *16*, 1435.
73. Zhang, T.; Chen, W.; Jiang, X.; Liu, L.; Wei, K.; Du, H.; Wang, H.; Li, J. Anticancer effects and underlying mechanism of Colchicine on human gastric cancer cell lines In Vitro and In Vivo. *Biosci. Rep.* **2019**, *39*, BSR20181802. [CrossRef]
74. Cho, J.H.; Joo, Y.H.; Shin, E.Y.; Park, E.J.; Kim, M.S. Anticancer effects of colchicine on hypopharyngeal cancer. *Anticancer Res.* **2017**, *37*, 6269–6280.
75. Bakar-Ateş, F.; Özmen, N.; Kaya-Sezginer, E.; Kurt, E.E. Effects of colchicine on cell cycle arrest and MMP-2 mRNA expression in MCF-7 breast adenocarcinoma cells. *Turk. Hij. Den. Biyol. Derg* **2018**, *75*, 239–244. [CrossRef]
76. Huang, Z.; Xu, Y.; Peng, W. Colchicine induces apoptosis in HT-29 human colon cancer cells via the AKT and c-Jun N-terminal kinase signaling pathways. *Mol. Med. Rep.* **2015**, *12*, 5939–5944. [CrossRef] [PubMed]
77. Boehle, A.S.; Sipos, B.; Kliche, U.; Kalthoff, H.; Dohrmann, P. Combretastatin A-4 prodrug inhibits growth of human non–small cell lung cancer in a murine xenotransplant model. *Ann. Thorac. Surg.* **2001**, *71*, 1657–1665. [CrossRef]
78. Shen, C.H.; Shee, J.J.; Wu, J.Y.; Lin, Y.W.; Wu, J.D.; Liu, Y.W. Combretastatin A-4 inhibits cell growth and metastasis in bladder cancer cells and retards tumour growth in a murine orthotopic bladder tumour model. *Br. J. Pharmacol.* **2010**, *160*, 2008–2027. [CrossRef] [PubMed]
79. Wang, H.; Li, W.; Xu, J.; Zhang, T.; Zuo, D.; Zhou, Z.; Lin, B.; Wang, G.; Wang, Z.; Sun, W. NDRG1 inhibition sensitizes osteosarcoma cells to combretastatin A-4 through targeting autophagy. *Cell Death Dis.* **2017**, *8*, e3048. [CrossRef]
80. Zhang, B.Y.; Zhang, L.; Chen, Y.M.; Qiao, X.; Zhao, S.L.; Li, P.; Liu, J.F.; Wen, X.; Yang, J. Corosolic acid inhibits colorectal cancer cells growth as a novel HER2/HER3 heterodimerization inhibitor. *Br. J. Pharmacol.* **2021**, *178*, 1475–1491. [CrossRef]
81. Park, J.B.; Lee, J.S.; Lee, M.S.; Cha, E.Y.; Kim, S.; Sul, J.Y. Corosolic acid reduces 5-FU chemoresistance in human gastric cancer cells by activating AMPK. *Mol. Med. Rep.* **2018**, *18*, 2880–2888. [CrossRef]
82. Zhang, C.; Niu, Y.; Wang, Z.; Xu, X.; Li, Y.; Ma, L.; Wang, J.; Yu, Y. Corosolic acid inhibits cancer progression by decreasing the level of CDK19-mediated O-GlcNAcylation in liver cancer cells. *Cell Death Dis.* **2021**, *12*, 1–11. [CrossRef]
83. Ma, B.; Zhang, H.; Wang, Y.; Zhao, A.; Zhu, Z.; Bao, X.; Sun, Y.; Li, L.; Zhang, Q. Corosolic acid, a natural triterpenoid, induces ER stress-dependent apoptosis in human castration resistant prostate cancer cells via activation of IRE-1/JNK, PERK/CHOP and TRIB3. *J. Exp. Clin. Cancer Res.* **2018**, *37*, 1–16. [CrossRef] [PubMed]
84. Xu, Y.Q.; Zhang, J.H.; Yang, X.S. Corosolic acid induces potent anti-cancer effects in CaSki cervical cancer cells through the induction of apoptosis, cell cycle arrest and PI3K/Akt signalling pathway. *Bangladesh J. Pharmacol.* **2016**, *11*, 453–459. [CrossRef]
85. Woo, S.M.; Seo, S.U.; Min, K.-j.; Im, S.-S.; Nam, J.-O.; Chang, J.-S.; Kim, S.; Park, J.-W.; Kwon, T.K. Corosolic acid induces non-apoptotic cell death through generation of lipid reactive oxygen species production in human renal carcinoma caki cells. *Int. J. Mol. Sci.* **2018**, *19*, 1309. [CrossRef] [PubMed]
86. Son, K.H.; Hwang, J.H.; Kim, D.H.; Cho, Y.-E. Effect of corosolic acid on apoptosis and angiogenesis in MDA-MB-231 human breast cancer cells. *J. Nutr. Health* **2020**, *53*, 111–120. [CrossRef]
87. Cui, A.; Li, X.; Ma, X.; Wang, X.; Liu, C.; Song, Z.; Pan, F.; Xia, Y.; Li, C. Transcriptome and Proteome Analysis Reveals Corosolic Acid Inhibiting Bladder Cancer via Targeting Cell Cycle and Inducing Mitophagy In Vitro and In Vivo. *Res. Sq.* **2021**. [CrossRef]
88. Festuccia, C.; Mancini, A.; Gravina, G.L.; Scarsella, L.; Llorens, S.; Alonso, G.L.; Tatone, C.; Di Cesare, E.; Jannini, E.A.; Lenzi, A. Antitumor effects of saffron-derived carotenoids in prostate cancer cell models. *BioMed Res. Int.* **2014**, *2014*, 135048. [CrossRef]
89. Ray, P.; Guha, D.; Chakraborty, J.; Banerjee, S.; Adhikary, A.; Chakraborty, S.; Das, T.; Sa, G. Crocetin exploits p53-induced death domain (PIDD) and FAS-associated death domain (FADD) proteins to induce apoptosis in colorectal cancer. *Sci. Rep.* **2016**, *6*, 1–11. [CrossRef]
90. Dhar, A.; Mehta, S.; Dhar, G.; Dhar, K.; Banerjee, S.; Van Veldhuizen, P.; Campbell, D.R.; Banerjee, S.K. Crocetin inhibits pancreatic cancer cell proliferation and tumor progression in a xenograft mouse model. *Mol. Cancer Ther.* **2009**, *8*, 315–323. [CrossRef]
91. Bathaie, S.Z.; Hoshyar, R.; Miri, H.; Sadeghizadeh, M. Anticancer effects of crocetin in both human adenocarcinoma gastric cancer cells and rat model of gastric cancer. *Biochem. Cell Biol.* **2013**, *91*, 397–403. [CrossRef]

92. Chai, Y.; Xiang, K.; Wu, Y.; Zhang, T.; Liu, Y.; Liu, X.; Zhen, W.; Si, Y. Cucurbitacin B inhibits the Hippo-YAP signaling pathway and exerts anticancer activity in colorectal cancer cells. *Med. Sci. Monit.* **2018**, *24*, 9251. [CrossRef]
93. Si, W.; Lyu, J.; Liu, Z.; Wang, C.; Huang, J.; Jiang, L.; Ma, T. Cucurbitacin E inhibits cellular proliferation and enhances the chemo-response in gastric cancer by suppressing AKt activation. *J. Cancer* **2019**, *10*, 5843. [CrossRef] [PubMed]
94. Obchoei, S.; Wongkham, S.; Aroonkesorn, A.; Suebsakwong, P.; Suksamrarn, A. Anti-cancer effect of cucurbitacin B on cholangiocarcinoma cells. *BMB* **2018**. [CrossRef]
95. Ku, J.M.; Hong, S.H.; Kim, H.I.; Lim, Y.S.; Lee, S.J.; Kim, M.; Seo, H.S.; Shin, Y.C.; Ko, S.-G. Cucurbitacin D exhibits its anti-cancer effect in human breast cancer cells by inhibiting Stat3 and Akt signaling. *Eur. J. Inflam.* **2018**, *16*, 1721727X17751809. [CrossRef]
96. Wang, X.; Hang, Y.; Liu, J.; Hou, Y.; Wang, N.; Wang, M. Anticancer effect of curcumin inhibits cell growth through miR-21/PTEN/Akt pathway in breast cancer cell. *Oncol. Lett.* **2017**, *13*, 4825–4831. [CrossRef]
97. Maulina, T.; Hadikrishna, I.; Hardianto, A.; Sjamsudin, E.; Pontjo, B.; Yusuf, H.Y. The therapeutic activity of curcumin through its anti-cancer potential on oral squamous cell carcinoma: A study on Sprague Dawley rat. *SAGE Open Med.* **2019**, *7*, 2050312119875982. [CrossRef]
98. Killian, P.H.; Kronski, E.; Michalik, K.M.; Barbieri, O.; Astigiano, S.; Sommerhoff, C.P.; Pfeffer, U.; Nerlich, A.G.; Bachmeier, B.E. Curcumin inhibits prostate cancer metastasis In Vivo by targeting the inflammatory cytokines CXCL1 and-2. *Carcinogenesis* **2012**, *33*, 2507–2519. [CrossRef]
99. Tong, W.; Wang, Q.; Sun, D.; Suo, J. Curcumin suppresses colon cancer cell invasion via AMPK-induced inhibition of NF-κB, uPA activator and MMP9. *Oncol. Lett.* **2016**, *12*, 4139–4146. [CrossRef]
100. Kim, M.J.; Park, K.-S.; Kim, K.-T.; Gil, E.Y. The inhibitory effect of curcumin via fascin suppression through JAK/STAT3 pathway on metastasis and recurrence of ovary cancer cells. *BMC Womens Health* **2020**, *20*, 1–9. [CrossRef]
101. Tang, L.; Liu, J.; Zhu, L.; Chen, Q.; Meng, Z.; Sun, L.; Hu, J.; Ni, Z.; Wang, X. Curcumin inhibits growth of human NCI-H292 lung squamous cell carcinoma cells by increasing FOXA2 expression. *Front. Pharmacol.* **2018**, *9*, 60. [CrossRef]
102. Liu, Y.; Zhou, Z.; Yan, J.; Wu, X.; Xu, G. Diosgenin exerts antitumor activity via downregulation of Skp2 in breast cancer cells. *Biomed Res. Int.* **2020**, *2020*, 8072639. [CrossRef]
103. Li, Y.; Wang, X.; Cheng, S.; Du, J.; Deng, Z.; Zhang, Y.; Liu, Q.; Gao, J.; Cheng, B.; Ling, C. Diosgenin induces G2/M cell cycle arrest and apoptosis in human hepatocellular carcinoma cells. *Oncol. Rep.* **2015**, *33*, 693–698. [CrossRef] [PubMed]
104. Jia, S.-S.; Xi, G.-P.; Zhang, M.; Chen, Y.-B.; Lei, B.; Dong, X.-S.; Yang, Y.-M. Induction of apoptosis by D-limonene is mediated by inactivation of Akt in LS174T human colon cancer cells. *Oncol. Rep.* **2013**, *29*, 349–354. [CrossRef] [PubMed]
105. Yu, X.; Lin, H.; Wang, Y.; Lv, W.; Zhang, S.; Qian, Y.; Deng, X.; Feng, N.; Yu, H.; Qian, B. D-limonene exhibits antitumor activity by inducing autophagy and apoptosis in lung cancer. *Onco Targets Ther.* **2018**, *11*, 1833. [CrossRef] [PubMed]
106. Rabi, T.; Bishayee, A. d-Limonene sensitizes docetaxel-induced cytotoxicity in human prostate cancer cells: Generation of reactive oxygen species and induction of apoptosis. *J. Carcinog.* **2009**, *8*. [CrossRef]
107. Zhang, N.; Wang, J.; Sheng, A.; Huang, S.; Tang, Y.; Ma, S.; Hong, G. Emodin Inhibits the proliferation of MCF-7 human breast cancer cells through activation of aryl hydrocarbon receptor (AhR). *Front. Pharmacol.* **2021**, *2372*. [CrossRef]
108. Li, M.; Jin, S.; Cao, Y.; Xu, J.; Zhu, S.; Li, Z. Emodin regulates cell cycle of non-small lung cancer (NSCLC) cells through hyaluronan synthase 2 (HA2)-HA-CD44/receptor for hyaluronic acid-mediated motility (RHAMM) interaction-dependent signaling pathway. *Cancer Cell Int.* **2021**, *21*, 1–12. [CrossRef]
109. Lin, S.-Z.; Wei, W.-T.; Chen, H.; Chen, K.-J.; Tong, H.-F.; Wang, Z.-H.; Ni, Z.-L.; Liu, H.-B.; Guo, H.-C.; Liu, D.-L. Antitumor activity of emodin against pancreatic cancer depends on its dual role: Promotion of apoptosis and suppression of angiogenesis. *PLoS ONE* **2012**, *7*, e42146. [CrossRef]
110. Saunders, I.T.; Mir, H.; Kapur, N.; Singh, S. Emodin inhibits colon cancer by altering BCL-2 family proteins and cell survival pathways. *Cancer Cell Int.* **2019**, *19*, 1–15. [CrossRef]
111. Deng, G.; Ju, X.; Meng, Q.; Yu, Z.J.; Ma, L.B. Emodin inhibits the proliferation of PC3 prostate cancer cells In Vitro via the Notch signaling pathway. *Mol. Med. Rep.* **2015**, *12*, 4427–4433. [CrossRef]
112. Kwak, T.W.; Park, S.B.; Kim, H.-J.; Jeong, Y.-I.; Kang, D.H. Anticancer activities of epigallocatechin-3-gallate against cholangiocarcinoma cells. *Onco Targets Ther.* **2017**, *10*, 137. [CrossRef]
113. Chen, B.-H.; Hsieh, C.-H.; Tsai, S.-Y.; Wang, C.-Y.; Wang, C.-C. Anticancer effects of epigallocatechin-3-gallate nanoemulsion on lung cancer cells through the activation of AMP-activated protein kinase signaling pathway. *Sci. Rep.* **2020**, *10*, 1–11. [CrossRef] [PubMed]
114. Rao, S.D.; Pagidas, K. Epigallocatechin-3-gallate, a natural polyphenol, inhibits cell proliferation and induces apoptosis in human ovarian cancer cells. *Anticancer Res.* **2010**, *30*, 2519–2523. [PubMed]
115. Moses, M.A.; Henry, E.C.; Ricke, W.A.; Gasiewicz, T.A. The heat shock protein 90 inhibitor,(−)-epigallocatechin gallate, has anticancer activity in a novel human prostate cancer progression model. *Cancer Prev. Res.* **2015**, *8*, 249–257. [CrossRef] [PubMed]
116. Shin, Y.S.; Kang, S.U.; Park, J.K.; Kim, Y.E.; Kim, Y.S.; Baek, S.J.; Lee, S.-H.; Kim, C.-H. Anti-cancer effect of (−)-epigallocatechin-3-gallate (EGCG) in head and neck cancer through repression of transactivation and enhanced degradation of β-catenin. *Phytomedicine* **2016**, *23*, 1344–1355. [CrossRef]
117. Md Nesran, Z.N.; Shafie, N.H.; Ishak, A.H.; Mohd Esa, N.; Ismail, A.; Md Tohid, S.F. Induction of endoplasmic reticulum stress pathway by green tea epigallocatechin-3-gallate (EGCG) in colorectal cancer cells: Activation of PERK/p-eIF2α/ATF4 and IRE1α. *Biomed Res. Int.* **2019**, *2019*. [CrossRef]

118. Xu, Y.; Fang, R.; Shao, J.; Cai, Z. Erianin induces triple-negative breast cancer cells apoptosis by activating PI3K/Akt pathway. *Biosci. Rep.* **2021**, *41*, BSR20210093. [CrossRef]
119. Chen, P.; Wu, Q.; Feng, J.; Yan, L.; Sun, Y.; Liu, S.; Xiang, Y.; Zhang, M.; Pan, T.; Chen, X. Erianin, a novel dibenzyl compound in Dendrobium extract, inhibits lung cancer cell growth and migration via calcium/calmodulin-dependent ferroptosis. *Signal Transduct. Target. Ther.* **2020**, *5*, 1–11. [CrossRef]
120. Chen, Y.-T.; Hsieh, M.-J.; Chen, P.-N.; Weng, C.-J.; Yang, S.-F.; Lin, C.-W. Erianin induces apoptosis and autophagy in oral squamous cell carcinoma cells. *Am. J. Chin. Med.* **2020**, *48*, 183–200. [CrossRef]
121. Zhu, Q.; Sheng, Y.; Li, W.; Wang, J.; Ma, Y.; Du, B.; Tang, Y. Erianin, a novel dibenzyl compound in Dendrobium extract, inhibits bladder cancer cell growth via the mitochondrial apoptosis and JNK pathways. *Toxicol. Appl. Pharmacol.* **2019**, *371*, 41–54. [CrossRef]
122. Wang, H.; Zhang, T.; Sun, W.; Wang, Z.; Zuo, D.; Zhou, Z.; Li, S.; Xu, J.; Yin, F.; Hua, Y. Erianin induces G2/M-phase arrest, apoptosis, and autophagy via the ROS/JNK signaling pathway in human osteosarcoma cells In Vitro and In Vivo. *Cell Death Dis.* **2016**, *7*, e2247. [CrossRef]
123. Tang, J.; Liu, J.; Zhang, C.; Zhou, C.; Chen, J. Erianin induces apoptosis of colorectal cancer cells via activation of JNK signaling pathways. *Int. J. Clin. Exp. Med.* **2019**, *12*, 11404–11411.
124. Li, M.; He, Y.; Peng, C.; Xie, X.; Hu, G. Erianin inhibits human cervical cancer cell through regulation of tumor protein p53 via the extracellular signal-regulated kinase signaling pathway. *Oncol. Lett.* **2018**, *16*, 5006–5012. [CrossRef] [PubMed]
125. Jiang, Z.-B.; Huang, J.-M.; Xie, Y.-J.; Zhang, Y.-Z.; Chang, C.; Lai, H.-L.; Wang, W.; Yao, X.-J.; Fan, X.-X.; Wu, Q.-B. Evodiamine suppresses non-small cell lung cancer by elevating CD8+ T cells and downregulating the MUC1-C/PD-L1 axis. *J. Exp. Clin. Cancer Res.* **2020**, *39*, 1–16. [CrossRef]
126. Chen, M.C.; Yu, C.H.; Wang, S.W.; Pu, H.F.; Kan, S.F.; Lin, L.C.; Chi, C.W.; Ho, L.L.T.; Lee, C.H.; Wang, P.S. Anti-proliferative effects of evodiamine on human thyroid cancer cell line ARO. *J. Cell. Biochem.* **2010**, *110*, 1495–1503. [CrossRef] [PubMed]
127. Kan, S.F.; Yu, C.H.; Pu, H.F.; Hsu, J.M.; Chen, M.J.; Wang, P.S. Anti-proliferative effects of evodiamine on human prostate cancer cell lines DU145 and PC3. *J. Cell. Biochem.* **2007**, *101*, 44–56. [CrossRef] [PubMed]
128. Jia, J.; Kang, X.; Liu, Y.; Zhang, J. Inhibition of human liver cancer cell growth by evodiamine involves apoptosis and deactivation of PI3K/AKT pathway. *Appl. Biol. Chem.* **2020**, *63*, 1–8. [CrossRef]
129. Shi, C.-S.; Li, J.-M.; Chin, C.-C.; Kuo, Y.-H.; Lee, Y.-R.; Huang, Y.-C. Evodiamine induces cell growth arrest, apoptosis and suppresses tumorigenesis in human urothelial cell carcinoma cells. *Anticancer Res.* **2017**, *37*, 1149–1159.
130. Zhou, P.; Li, X.-P.; Jiang, R.; Chen, Y.; Lv, X.-T.; Guo, X.-X.; Tian, K.; Yuan, D.-Z.; Lv, Y.-W.; Ran, J.-H. Evodiamine inhibits migration and invasion by Sirt1-mediated post-translational modulations in colorectal cancer. *Anticancer Drugs* **2019**, *30*, 611. [CrossRef]
131. Zhong, Z.-F.; Tan, W.; Wang, S.-P.; Qiang, W.-A.; Wang, Y.-T. Anti-proliferative activity and cell cycle arrest induced by evodiamine on paclitaxel-sensitive and-resistant human ovarian cancer cells. *Sci. Rep.* **2015**, *5*, 1–12. [CrossRef]
132. Khan, M.; Qazi, J.I.; Rasul, A.; Zheng, Y.; Ma, T. Evodiamine induces apoptosis in pancreatic carcinoma PANC-1 cells via NF-κB inhibition. *Bangladesh J. Pharmacol.* **2013**, *8*, 8–14. [CrossRef]
133. Wang, S.; Wang, K.; Wang, H.; Han, J.; Sun, H. Autophagy is essential for flavopiridol-induced cytotoxicity against MCF-7 breast cancer cells. *Mol. Med. Rep.* **2017**, *16*, 9715–9720. [CrossRef] [PubMed]
134. Pinto, N.; Prokopec, S.D.; Ghasemi, F.; Meens, J.; Ruicci, K.M.; Khan, I.M.; Mundi, N.; Patel, K.; Han, M.W.; Yoo, J. Flavopiridol causes cell cycle inhibition and demonstrates anti-cancer activity in anaplastic thyroid cancer models. *PLoS ONE* **2020**, *15*, e0239315. [CrossRef] [PubMed]
135. Saisomboon, S.; Kariya, R.; Vaeteewoottacharn, K.; Wongkham, S.; Sawanyawisuth, K.; Okada, S. Antitumor effects of flavopiridol, a cyclin-dependent kinase inhibitor, on human cholangiocarcinoma In Vitro and in an In Vivo xenograft model. *Heliyon* **2019**, *5*, e01675. [CrossRef] [PubMed]
136. Patel, V.; Senderowicz, A.M.; Pinto, D.; Igishi, T.; Raffeld, M.; Quintanilla-Martinez, L.; Ensley, J.F.; Sausville, E.A.; Gutkind, J.S. Flavopiridol, a novel cyclin-dependent kinase inhibitor, suppresses the growth of head and neck squamous cell carcinomas by inducing apoptosis. *J. Clin. Investig.* **1998**, *102*, 1674–1681. [CrossRef]
137. Cetintas, V.B.; Acikgoz, E.; Yigitturk, G.; Demir, K.; Oktem, G.; Kaymaz, B.T.; Oltulu, F.; Aktug, H. Effects of flavopiridol on critical regulation pathways of CD133high/CD44high lung cancer stem cells. *Medicine* **2016**, *95*. [CrossRef]
138. Hassan, M.S.; Cwidak, N.; Johnson, C.; Däster, S.; Eppenberger-Castori, S.; Awasthi, N.; Li, J.; Schwarz, M.A.; von Holzen, U. Therapeutic Potential of the Cyclin-Dependent Kinase Inhibitor Flavopiridol on c-Myc Overexpressing Esophageal Cancer. *Front. Pharmacol.* **2021**, *2589*. [CrossRef]
139. Ko, E.-B.; Jang, Y.-G.; Kim, C.-W.; Go, R.-E.; Lee, H.K.; Choi, K.-C. Gallic Acid Hindered Lung Cancer Progression by Inducing Cell Cycle Arrest and Apoptosis in A549 Lung Cancer Cells via PI3K/Akt Pathway. *Biomol. Ther.* **2021**, *30*, 151–161. [CrossRef]
140. Shi, C.-j.; Zheng, Y.B.; Pan, F.F.; Zhang, F.W.; Zhuang, P.; Fu, W.M. Gallic Acid Suppressed Tumorigenesis by an LncRNA MALAT1-Wnt/β-Catenin Axis in Hepatocellular Carcinoma. *Front. Pharmacol.* **2021**, *12*. [CrossRef]
141. Moghtaderi, H.; Sepehri, H.; Delphi, L.; Attari, F. Gallic acid and curcumin induce cytotoxicity and apoptosis in human breast cancer cell MDA-MB-231. *BioImpacts BI* **2018**, *8*, 185. [CrossRef]
142. Lin, X.; Wang, G.; Liu, P.; Han, L.; Wang, T.; Chen, K.; Gao, Y. Gallic acid suppresses colon cancer proliferation by inhibiting SRC and EGFR phosphorylation. *Exp. Ther. Med.* **2021**, *21*, 1–11. [CrossRef]

143. Tsai, C.-L.; Chiu, Y.-M.; Ho, T.-Y.; Hsieh, C.-T.; Shieh, D.-C.; Lee, Y.-J.; Tsay, G.J.; Wu, Y.-Y. Gallic acid induces apoptosis in human gastric adenocarcinoma cells. *Anticancer Res.* **2018**, *38*, 2057–2067. [PubMed]
144. Chen, H.-M.; Wu, Y.-C.; Chia, Y.-C.; Chang, F.-R.; Hsu, H.-K.; Hsieh, Y.-C.; Chen, C.-C.; Yuan, S.-S. Gallic acid, a major component of Toona sinensis leaf extracts, contains a ROS-mediated anti-cancer activity in human prostate cancer cells. *Cancer Lett.* **2009**, *286*, 161–171. [CrossRef] [PubMed]
145. Varela-Rodríguez, L.; Sánchez-Ramírez, B.; Hernández-Ramírez, V.I.; Varela-Rodríguez, H.; Castellanos-Mijangos, R.D.; González-Horta, C.; Chávez-Munguía, B.; Talamás-Rohana, P. Effect of Gallic acid and Myricetin on ovarian cancer models: A possible alternative antitumoral treatment. *BMC Complement. Med. Ther.* **2020**, *20*, 1–16. [CrossRef] [PubMed]
146. Liu, Z.; Li, D.; Yu, L.; Niu, F. Gallic acid as a cancer-selective agent induces apoptosis in pancreatic cancer cells. *Chemotherapy* **2012**, *58*, 185–194. [CrossRef] [PubMed]
147. Hatami, E.; Nagesh, P.K.; Jaggi, M.; Chauhan, S.C.; Yallapu, M.M. Gambogic acid potentiates gemcitabine induced anticancer activity in non-small cell lung cancer. *Eur. J. Pharmacol.* **2020**, *888*, 173486. [CrossRef]
148. Zhou, J.; Luo, Y.-H.; Wang, J.-R.; Lu, B.-B.; Wang, K.-M.; Tian, Y. Gambogenic acid induction of apoptosis in a breast cancer cell line. *Asian Pac. J. Cancer Prev.* **2013**, *14*, 7601–7605. [CrossRef]
149. Lee, P.N.H.; Ho, W.S. Antiproliferative activity of gambogic acid isolated from Garcinia hanburyi in Hep3B and Huh7 cancer cells. *Oncol. Rep.* **2013**, *29*, 1744–1750. [CrossRef]
150. Pan, H.; Jansson, K.H.; Beshiri, M.L.; Yin, J.; Fang, L.; Agarwal, S.; Nguyen, H.; Corey, E.; Zhang, Y.; Liu, J. Gambogic acid inhibits thioredoxin activity and induces ROS-mediated cell death in castration-resistant prostate cancer. *Oncotarget* **2017**, *8*, 77181. [CrossRef]
151. Zhang, H.; Lei, Y.; Yuan, P.; Li, L.; Luo, C.; Gao, R.; Tian, J.; Feng, Z.; Nice, E.C.; Sun, J. ROS-mediated autophagy induced by dysregulation of lipid metabolism plays a protective role in colorectal cancer cells treated with gambogic acid. *PLoS ONE* **2014**, *9*, e96418. [CrossRef]
152. Lin, D.; Lin, X.; He, T.; Xie, G. Gambogic Acid Inhibits the Progression of Gastric Cancer via circRNA_ASAP2/miR-33a-5p/CDK7 Axis. *Cancer Manag. Res.* **2020**, *12*, 9221. [CrossRef]
153. Zhang, Q.; Bao, J.; Yang, J. Genistein-triggered anticancer activity against liver cancer cell line HepG2 involves ROS generation, mitochondrial apoptosis, G2/M cell cycle arrest and inhibition of cell migration. *Arch. Med. Sci.* **2019**, *15*, 1001. [CrossRef] [PubMed]
154. Qin, J.; Chen, J.X.; Zhu, Z.; Teng, J.A. Genistein inhibits human colorectal cancer growth and suppresses miR-95, Akt and SGK1. *Cell. Physiol. Biochem.* **2015**, *35*, 2069–2077. [CrossRef] [PubMed]
155. Pavese, J.M.; Krishna, S.N.; Bergan, R.C. Genistein inhibits human prostate cancer cell detachment, invasion, and metastasis. *Am. J. Clin. Nutr.* **2014**, *100*, 431S–436S. [CrossRef] [PubMed]
156. Fu, Z.; Cao, X.; Liu, L.; Cao, X.; Cui, Y.; Li, X.; Quan, M.; Ren, K.; Chen, A.; Xu, C. Genistein inhibits lung cancer cell stem-like characteristics by modulating MnSOD and FoxM1 expression. *Oncol. Lett.* **2020**, *20*, 2506–2515. [CrossRef]
157. Sp, N.; Kang, D.Y.; Lee, J.-M.; Bae, S.W.; Jang, K.-J. Potential antitumor effects of 6-gingerol in p53-dependent mitochondrial apoptosis and inhibition of tumor sphere formation in breast cancer cells. *Int. J. Mol. Sci.* **2021**, *22*, 4660. [CrossRef]
158. Kapoor, V.; Aggarwal, S.; Das, S.N. 6-Gingerol mediates its anti tumor activities in human oral and cervical cancer cell lines through apoptosis and cell cycle arrest. *Phytother. Res.* **2016**, *30*, 588–595. [CrossRef]
159. Tsai, Y.; Xia, C.; Sun, Z. The Inhibitory Effect of 6-Gingerol on Ubiquitin-Specific Peptidase 14 Enhances Autophagy-Dependent Ferroptosis and Anti-Tumor In Vivo and In Vitro. *Front. Pharmacol.* **2020**, *11*, 1792. [CrossRef]
160. Park, Y.J.; Wen, J.; Bang, S.; Park, S.W.; Song, S.Y. [6]-Gingerol induces cell cycle arrest and cell death of mutant p53-expressing pancreatic cancer cells. *Yonsei Med. J.* **2006**, *47*, 688–697. [CrossRef]
161. Park, Y.; Woo, S.H.; Seo, S.K.; Kim, H.; Noh, W.C.; Lee, J.K.; Kwon, B.M.; Min, K.N.; Choe, T.B.; Park, I.C. Ginkgetin induces cell death in breast cancer cells via downregulation of the estrogen receptor. *Oncol. Lett.* **2017**, *14*, 5027–5033. [CrossRef]
162. Lou, J.-S.; Bi, W.-C.; Chan, G.K.; Jin, Y.; Wong, C.-W.; Zhou, Z.-Y.; Wang, H.-Y.; Yao, P.; Dong, T.T.; Tsim, K.W. Ginkgetin induces autophagic cell death through p62/SQSTM1-mediated autolysosome formation and redox setting in non-small cell lung cancer. *Oncotarget* **2017**, *8*, 93131. [CrossRef]
163. Jeon, Y.J.; Jung, S.N.; Yun, J.; Lee, C.W.; Choi, J.; Lee, Y.J.; Han, D.C.; Kwon, B.M. Ginkgetin inhibits the growth of DU− 145 prostate cancer cells through inhibition of signal transducer and activator of transcription 3 activity. *Cancer Sci.* **2015**, *106*, 413–420. [CrossRef] [PubMed]
164. Xiong, M.; Wang, L.; Yu, H.L.; Han, H.; Mao, D.; Chen, J.; Zeng, Y.; He, N.; Liu, Z.G.; Wang, Z.Y. Ginkgetin exerts growth inhibitory and apoptotic effects on osteosarcoma cells through inhibition of STAT3 and activation of caspase-3/9. *Oncol. Rep.* **2016**, *35*, 1034–1040. [CrossRef] [PubMed]
165. Su, Y.; Sun, C.-M.; Chuang, H.-H.; Chang, P.-T. Studies on the cytotoxic mechanisms of ginkgetin in a human ovarian adenocarcinoma cell line. *Naunyn-Schmiedeberg's Arch. Pharmacol.* **2000**, *362*, 82–90. [CrossRef] [PubMed]
166. Ren, Y.; Huang, S.S.; Wang, X.; Lou, Z.G.; Yao, X.P.; Weng, G.B. Ginkgetin induces apoptosis in 786-O cell line via suppression of JAK2-STAT3 pathway. *Iran. J. Basic Med. Sci.* **2016**, *19*, 1245.
167. Lin, S.-C.; Chu, P.-Y.; Liao, W.-T.; Wu, M.-Y.; Tsui, K.-H.; Lin, L.-T.; Huang, C.-H.; Chen, L.-L.; Li, C.-J. Glycyrrhizic acid induces human MDA-MB-231 breast cancer cell death and autophagy via the ROS-mitochondrial pathway. *Oncol. Rep.* **2018**, *39*, 703–710. [CrossRef]

168. Wang, H.; Ge, X.; Qu, H.; Wang, N.; Zhou, J.; Xu, W.; Xie, J.; Zhou, Y.; Shi, L.; Qin, Z. Glycyrrhizic Acid Inhibits Proliferation of Gastric Cancer Cells by Inducing Cell Cycle Arrest and Apoptosis. *Cancer Manag. Res.* **2020**, *12*, 2853. [CrossRef]
169. Thirugnanam, S.; Xu, L.; Ramaswamy, K.; Gnanasekar, M. Glycyrrhizin induces apoptosis in prostate cancer cell lines DU-145 and LNCaP. *Oncol. Rep.* **2008**, *20*, 1387–1392.
170. Haghshenas, V.; Fakhari, S.; Mirzaie, S.; Rahmani, M.; Farhadifar, F.; Pirzadeh, S.; Jalili, A. Glycyrrhetinic Acid inhibits cell growth and induces apoptosis in ovarian cancer a2780 cells. *Adv. Pharm. Bull.* **2014**, *4*, 437.
171. Cao, H.; Sethumadhavan, K.; Cao, F.; Wang, T.T. Gossypol decreased cell viability and down-regulated the expression of a number of genes in human colon cancer cells. *Sci. Rep.* **2021**, *11*, 1–16. [CrossRef]
172. Messeha, S.S.; Zarmouh, N.O.; Mendonca, P.; Cotton, C.; Soliman, K.F. Molecular mechanism of gossypol mediating CCL2 and IL-8 attenuation in triple-negative breast cancer cells. *Mol. Med. Rep.* **2020**, *22*, 1213–1226. [CrossRef]
173. Wang, Y.; Lai, H.; Fan, X.; Luo, L.; Duan, F.; Jiang, Z.; Wang, Q.; Leung, E.L.H.; Liu, L.; Yao, X. Gossypol inhibits non-small cell lung cancer cells proliferation by targeting EGFRL858R/T790M. *Front. Pharmacol.* **2018**, *9*, 728. [CrossRef] [PubMed]
174. Volate, S.R.; Kawasaki, B.T.; Hurt, E.M.; Milner, J.A.; Kim, Y.S.; White, J.; Farrar, W.L. Gossypol Induces Apoptosis by Activating p53 in Prostate Cancer Cells and Prostate Tumor–Initiating Cells. *Mol. Cancer Ther.* **2010**, *9*, 461–470. [CrossRef] [PubMed]
175. Wang, J.; Jin, L.; Li, X.; Deng, H.; Chen, Y.; Lian, Q.; Ge, R.; Deng, H. Gossypol induces apoptosis in ovarian cancer cells through oxidative stress. *Mol. Biosyst.* **2013**, *9*, 1489–1497. [CrossRef] [PubMed]
176. Hsieh, Y.-S.; Chu, S.-C.; Huang, S.-C.; Kao, S.-H.; Lin, M.-S.; Chen, P.-N. Gossypol Reduces Metastasis and Epithelial-Mesenchymal Transition by Targeting Protease in Human Cervical Cancer. *Am. J. Chin. Med.* **2021**, *49*, 181–198. [CrossRef]
177. Wolter, K.G.; Wang, S.J.; Henson, B.S.; Wang, S.; Griffith, K.A.; Kumar, B.; Chen, J.; Carey, T.E.; Bradford, C.R.; D'Silva, N.J. (−)-gossypol inhibits growth and promotes apoptosis of human head and neck squamous cell carcinoma In Vivo. *Neoplasia* **2006**, *8*, 163–172. [CrossRef]
178. Haasler, L.; Kondadi, A.K.; Tsigaras, T.; von Montfort, C.; Graf, P.; Stahl, W.; Brenneisen, P. The BH3 mimetic (±) gossypol induces ROS-independent apoptosis and mitochondrial dysfunction in human A375 melanoma cells In Vitro. *Arch. Toxicol.* **2021**, *95*, 1349–1365. [CrossRef]
179. Ding, Y.; He, J.; Huang, J.; Yu, T.; Shi, X.; Zhang, T.; Yan, G.; Chen, S.; Peng, C. Harmine induces anticancer activity in breast cancer cells via targeting TAZ. *Int. J. Oncol.* **2019**, *54*, 1995–2004. [CrossRef]
180. Ruan, S.; Jia, F.; Li, J. Potential antitumor effect of harmine in the treatment of thyroid cancer. *Evid. Based Complement. Alternat. Med.* **2017**, *2017*. [CrossRef]
181. Li, C.; Wang, Y.; Wang, C.; Yi, X.; Li, M.; He, X. Anticancer activities of harmine by inducing a pro-death autophagy and apoptosis in human gastric cancer cells. *Phytomedicine* **2017**, *28*, 10–18. [CrossRef]
182. Wu, L.-W.; Zhang, J.-K.; Rao, M.; Zhang, Z.-Y.; Zhu, H.-J.; Zhang, C. Harmine suppresses the proliferation of pancreatic cancer cells and sensitizes pancreatic cancer to gemcitabine treatment. *Onco Targets Ther.* **2019**, *12*, 4585. [CrossRef]
183. Gao, J.; Zhu, H.; Wan, H.; Zou, X.; Ma, X.; Gao, G. Harmine suppresses the proliferation and migration of human ovarian cancer cells through inhibiting ERK/CREB pathway. *Oncol. Rep.* **2017**, *38*, 2927–2934. [CrossRef] [PubMed]
184. Zhang, X.-F.; Sun, R.Q.; Jia, Y.F.; Chen, Q.; Tu, R.-F.; Li, K.K.; Zhang, X.-D.; Du, R.-L.; Cao, R.H. Synthesis and mechanisms of action of novel harmine derivatives as potential antitumor agents. *Sci. Rep.* **2016**, *6*, 1–16. [CrossRef] [PubMed]
185. Cincin, Z.B.; Unlu, M.; Kiran, B.; Bireller, E.S.; Baran, Y.; Cakmakoglu, B. Anti-proliferative, apoptotic and signal transduction effects of hesperidin in non-small cell lung cancer cells. *Cell. Oncol.* **2015**, *38*, 195–204. [CrossRef]
186. Banjerdpongchai, R.; Wudtiwai, B.; Khaw-On, P.; Rachakhom, W.; Duangnil, N.; Kongtawelert, P. Hesperidin from Citrus seed induces human hepatocellular carcinoma HepG2 cell apoptosis via both mitochondrial and death receptor pathways. *Tumor Biol.* **2016**, *37*, 227–237. [CrossRef] [PubMed]
187. Zhao, W.; Chen, Y.; Zhang, X. Hesperidin-triggered necrosis-like cell death in skin cancer cell line A431 might be prompted by ROS mediated alterations in mitochondrial membrane potential. *Int. J. Clin. Exp. Med.* **2018**, *11*, 1948–1954.
188. Ning, L.; Zhao, W.; Gao, H.; Wu, Y. Hesperidin induces anticancer effects on human prostate cancer cells via ROS-mediated necrosis like cell death. *J. BUON* **2020**, *25*, 2629–2634.
189. Kongtawelert, P.; Wudtiwai, B.; Shwe, T.H.; Pothacharoen, P.; Phitak, T. Inhibitory effect of Hesperidin on the expression of programmed death ligand (PD-L1) in breast Cancer. *Molecules* **2020**, *25*, 252. [CrossRef]
190. Lv, L.; Zhang, W.; Li, T.; Jiang, L.; Lu, X.; Lin, J. Hispidulin exhibits potent anticancer activity In Vitro and In Vivo through activating ER stress in non-small-cell lung cancer cells. *Oncol. Rep.* **2020**, *43*, 1995–2003. [CrossRef]
191. Han, M.; Gao, H.; Ju, P.; Gao, M.Q.; Yuan, Y.P.; Chen, X.H.; Liu, K.L.; Han, Y.T.; Han, Z.W. Hispidulin inhibits hepatocellular carcinoma growth and metastasis through AMPK and ERK signaling mediated activation of PPARγ. *Biomed. Pharmacother.* **2018**, *103*, 272–283. [CrossRef]
192. Gao, H.; Gao, M.Q.; Peng, J.J.; Han, M.; Liu, K.L.; Han, Y.T. Hispidulin mediates apoptosis in human renal cell carcinoma by inducing ceramide accumulation. *Acta Pharmacol. Sin.* **2017**, *38*, 1618–1631. [CrossRef]
193. Yu, C.Y.; Su, K.-Y.; Lee, P.-L.; Jhan, J.-Y.; Tsao, P.-H.; Chan, D.-C.; Chen, Y.-L.S. Potential therapeutic role of hispidulin in gastric cancer through induction of apoptosis via NAG-1 signaling. *Evid. Based Complement. Alternat. Med.* **2013**, *2013*, 518301. [CrossRef] [PubMed]
194. Zhu, L.; Xue, L. Kaempferol suppresses proliferation and induces cell cycle arrest, apoptosis, and DNA damage in breast cancer cells. *Oncol. Res.* **2019**, *27*, 629. [CrossRef] [PubMed]

195. Han, B.; Yu, Y.-Q.; Yang, Q.-L.; Shen, C.-Y.; Wang, X.-J. Kaempferol induces autophagic cell death of hepatocellular carcinoma cells via activating AMPK signaling. *Oncotarget* **2017**, *8*, 86227. [CrossRef] [PubMed]
196. Hung, T.-W.; Chen, P.-N.; Wu, H.-C.; Wu, S.-W.; Tsai, P.-Y.; Hsieh, Y.-S.; Chang, H.-R. Kaempferol inhibits the invasion and migration of renal cancer cells through the downregulation of AKT and FAK pathways. *Int. J. Med. Sci.* **2017**, *14*, 984. [CrossRef]
197. Tu, L.Y.; Bai, H.H.; Cai, J.Y.; Deng, S.P. The mechanism of kaempferol induced apoptosis and inhibited proliferation in human cervical cancer SiHa cell: From macro to nano. *Scanning* **2016**, *38*, 644–653. [CrossRef]
198. Wang, F.; Wang, L.; Qu, C.; Chen, L.; Geng, Y.; Cheng, C.; Yu, S.; Wang, D.; Yang, L.; Meng, Z. Kaempferol induces ROS-dependent apoptosis in pancreatic cancer cells via TGM2-mediated Akt/mTOR signaling. *BMC Cancer* **2021**, *21*, 1–11. [CrossRef]
199. Li, W.; Du, B.; Wang, T.; Wang, S.; Zhang, J. Kaempferol induces apoptosis in human HCT116 colon cancer cells via the Ataxia-Telangiectasia Mutated-p53 pathway with the involvement of p53 Upregulated Modulator of Apoptosis. *Chem. Biol. Interact.* **2009**, *177*, 121–127. [CrossRef]
200. Yang, J.; Chen, H.; Wang, Q.; Deng, S.; Huang, M.; Ma, X.; Song, P.; Du, J.; Huang, Y.; Wen, Y. Inhibitory effect of kurarinone on growth of human non-small cell lung cancer: An experimental study both In Vitro and In Vivo studies. *Front. Pharmacol.* **2018**, *9*, 252. [CrossRef]
201. Zhou, W.; Cao, A.; Wang, L.; Wu, D. Kurarinone synergizes TRAIL-induced apoptosis in gastric cancer cells. *Cell Biochem. Biophys.* **2015**, *72*, 241–249. [CrossRef]
202. De Naeyer, A.; Vanden Berghe, W.; Pocock, V.; Milligan, S.; Haegeman, G.; De Keukeleire, D. Estrogenic and Anticarcinogenic Properties of Kurarinone, a Lavandulyl Flavanone from the Roots of Sophora f lavescens. *J. Nat. Prod.* **2004**, *67*, 1829–1832. [CrossRef]
203. Qu, D.; Zhang, X.; Sang, C.; Zhou, Y.; Ma, J.; Hui, L. Lappaconitine sulfate induces apoptosis in human colon cancer HT-29 cells and down-regulates PI3K/AKT/GSK3β signaling pathway. *Med. Chem. Res.* **2019**, *28*, 907–916. [CrossRef]
204. Sheng, L.-H.; Xu, M.; Xu, L.-Q.; Xiong, F. Cytotoxic effect of lappaconitine on non-small cell lung cancer In Vitro and its molecular mechanism. *J. Chin. Med. Mater.* **2014**, *37*, 840–843.
205. Song, N.; Ma, J.; Zhang, X.; Qu, D.; Hui, L.; Sang, C.; Li, H. Lappaconitine hydrochloride induces apoptosis and S phase cell cycle arrest through MAPK signaling pathway in human liver cancer HepG2 cells. *Pharmacogn. Mag.* **2021**, *17*, 334.
206. Xue, L.; Zhang, W.J.; Fan, Q.X.; Wang, L.X. Licochalcone A inhibits PI3K/Akt/mTOR signaling pathway activation and promotes autophagy in breast cancer cells. *Oncol. Lett.* **2018**, *15*, 1869–1873. [CrossRef] [PubMed]
207. Yuan, X.; Li, D.; Zhao, H.; Jiang, J.; Wang, P.; Ma, X.; Sun, X.; Zheng, Q. Licochalcone A-induced human bladder cancer T24 cells apoptosis triggered by mitochondria dysfunction and endoplasmic reticulum stress. *Biomed Res. Int.* **2013**, *2013*, 911–919. [CrossRef] [PubMed]
208. Luo, W.; Sun, R.; Chen, X.; Li, J.; Jiang, J.; He, Y.; Shi, S.; Wen, H. ERK activation-mediated autophagy induction resists licochalcone A-induced anticancer activities in lung cancer cells In Vitro. *Onco Targets Ther.* **2020**, *13*, 13437. [CrossRef]
209. Tsai, J.-P.; Hsiao, P.-C.; Yang, S.-F.; Hsieh, S.-C.; Bau, D.-T.; Ling, C.-L.; Pai, C.-L.; Hsieh, Y.-H. Licochalcone A suppresses migration and invasion of human hepatocellular carcinoma cells through downregulation of MKK4/JNK via NF-κB mediated urokinase plasminogen activator expression. *PLoS ONE* **2014**, *9*, e86537. [CrossRef]
210. Li, Z.H.; Gao, J.; Hu, P.H.; Xiong, J.P. Anticancer effects of liriodenine on the cell growth and apoptosis of human breast cancer MCF-7 cells through the upregulation of p53 expression. *Oncol. Lett.* **2017**, *14*, 1979–1984. [CrossRef]
211. Chang, H.-C.; Chang, F.-R.; Wu, Y.-C.; Lai, Y.-H. Anti-cancer effect of liriodenine on human lung cancer cells. *Kaohsiung J. Med. Sci.* **2004**, *20*, 365–371. [CrossRef]
212. Nordin, N.; Majid, N.A.; Hashim, N.M.; Abd Rahman, M.; Hassan, Z.; Ali, H.M. Liriodenine, an aporphine alkaloid from Enicosanthellum pulchrum, inhibits proliferation of human ovarian cancer cells through induction of apoptosis via the mitochondrial signaling pathway and blocking cell cycle progression. *Drug Des. Devel. Ther.* **2015**, *9*, 1437.
213. Cao, Z.; Zhang, H.; Cai, X.; Fang, W.; Chai, D.; Wen, Y.; Chen, H.; Chu, F.; Zhang, Y. Luteolin promotes cell apoptosis by inducing autophagy in hepatocellular carcinoma. *Cell. Physiol. Biochem.* **2017**, *43*, 1803–1812. [CrossRef] [PubMed]
214. Kang, K.A.; Piao, M.J.; Hyun, Y.J.; Zhen, A.X.; Cho, S.J.; Ahn, M.J.; Yi, J.M.; Hyun, J.W. Luteolin promotes apoptotic cell death via upregulation of Nrf2 expression by DNA demethylase and the interaction of Nrf2 with p53 in human colon cancer cells. *Exp. Mol. Med.* **2019**, *51*, 1–14. [CrossRef] [PubMed]
215. Song, S.; Su, Z.; Xu, H.; Niu, M.; Chen, X.; Min, H.; Zhang, B.; Sun, G.; Xie, S.; Wang, H. Correction: Luteolin selectively kills STAT3 highly activated gastric cancer cells through enhancing the binding of STAT3 to SHP-1. *Cell Death Dis.* **2018**, *9*, 1. [CrossRef] [PubMed]
216. Park, B.-S.; Kil, J.-J.; Kang, H.-M.; Yu, S.-B.; Park, D.-B.; Park, J.-A.; Kim, I.-R. Luteolin Induces Apoptosis via Mitochondrial Pathway and Inhibits Invasion and Migration of Oral Squamous Cell Carcinoma by Suppressing Epithelial-Mesenchymal Transition Induced Transcription Factors. *Int. J. Oral Biol.* **2018**, *43*, 69–76. [CrossRef]
217. Huang, L.; Jin, K.; Lan, H. Luteolin inhibits cell cycle progression and induces apoptosis of breast cancer cells through downregulation of human telomerase reverse transcriptase. *Oncol. Lett.* **2019**, *17*, 3842–3850. [CrossRef]
218. Cai, X.; Lu, W.; Ye, T.; Lu, M.; Wang, J.; Huo, J.; Qian, S.; Wang, X.; Cao, P. The molecular mechanism of luteolin-induced apoptosis is potentially related to inhibition of angiogenesis in human pancreatic carcinoma cells. *Oncol. Rep.* **2012**, *28*, 1353–1361. [CrossRef]

219. Masraksa, W.; Tanasawet, S.; Hutamekalin, P.; Wongtawatchai, T.; Sukketsiri, W. Luteolin attenuates migration and invasion of lung cancer cells via suppressing focal adhesion kinase and non-receptor tyrosine kinase signaling pathway. *Nutr. Res. Pract.* **2020**, *14*, 127–133. [CrossRef]
220. Takeshima, M.; Ono, M.; Higuchi, T.; Chen, C.; Hara, T.; Nakano, S. Anti-proliferative and apoptosis-inducing activity of lycopene against three subtypes of human breast cancer cell lines. *Cancer Sci.* **2014**, *105*, 252–257. [CrossRef]
221. Jiang, L.-N.; Liu, Y.-B.; Li, B.-H. Lycopene exerts anti-inflammatory effect to inhibit prostate cancer progression. *Asian J. Androl.* **2019**, *21*, 80.
222. Cha, J.H.; Kim, W.K.; Ha, A.W.; Kim, M.H.; Chang, M.J. Anti-inflammatory effect of lycopene in SW480 human colorectal cancer cells. *Nutr. Res. Pract.* **2017**, *11*, 90–96. [CrossRef]
223. Jeong, Y.; Lim, J.W.; Kim, H. Lycopene inhibits reactive oxygen species-mediated NF-κB signaling and induces apoptosis in pancreatic cancer cells. *Nutrients* **2019**, *11*, 762. [CrossRef]
224. Cheng, J.; Miller, B.; Balbuena, E.; Eroglu, A. Lycopene protects against smoking-induced lung cancer by inducing base excision repair. *Antioxidants* **2020**, *9*, 643. [CrossRef] [PubMed]
225. Luo, C.; Wu, X.-G. Lycopene enhances antioxidant enzyme activities and immunity function in N-Methyl-N′-nitro-N-nitrosoguanidine–induced gastric cancer rats. *Int. J. Mol. Sci.* **2011**, *12*, 3340–3351. [CrossRef] [PubMed]
226. Aktepe, O.H.; Şahin, T.K.; Güner, G.; Arik, Z.; Yalçin, Ş. Lycopene sensitizes the cervical cancer cells to cisplatin via targeting nuclear factor NF-kappa B. *Turk. J. Med. Sci.* **2021**, *51*, 368–374. [CrossRef] [PubMed]
227. Zhou, X.; Burke, K.E.; Wang, Y.; Wei, H. Dietary lycopene protects SkH-1 mice against ultraviolet B-induced photocarcinogenesis. *J. Drugs Dermatol.* **2019**, *18*, 1244–1254.
228. Czarnik-Kwaśniak, J.; Kwaśniak, K.; Kwasek, P.; Świerzowska, E.; Strojewska, A.; Tabarkiewicz, J. The influence of lycopene,[6]-gingerol, and silymarin on the apoptosis on U-118MG glioblastoma cells In Vitro model. *Nutrients* **2020**, *12*, 96. [CrossRef] [PubMed]
229. Holzapfel, N.P.; Shokoohmand, A.; Wagner, F.; Landgraf, M.; Champ, S.; Holzapfel, B.M.; Clements, J.A.; Hutmacher, D.W.; Loessner, D. Lycopene reduces ovarian tumor growth and intraperitoneal metastatic load. *Am. J. Cancer Res.* **2017**, *7*, 1322.
230. Wang, J.; Xu, J.; Xing, G. Lycorine inhibits the growth and metastasis of breast cancer through the blockage of STAT3 signaling pathway. *Acta Biochim. Biophys. Sin.* **2017**, *49*, 771–779. [CrossRef]
231. Hu, M.; Peng, S.; He, Y.; Qin, M.; Cong, X.; Xing, Y.; Liu, M.; Yi, Z. Lycorine is a novel inhibitor of the growth and metastasis of hormone-refractory prostate cancer. *Oncotarget* **2015**, *6*, 15348. [CrossRef]
232. Sun, Y.; Wu, P.; Sun, Y.; Sharopov, F.S.; Yang, Q.; Chen, F.; Wang, P.; Liang, Z. Lycorine possesses notable anticancer potentials in on-small cell lung carcinoma cells via blocking Wnt/β-catenin signaling and epithelial-mesenchymal transition (EMT). *Biochem. Biophys. Res. Commun.* **2018**, *495*, 911–921. [CrossRef]
233. Liu, W.; Zhang, Q.; Tang, Q.; Hu, C.; Huang, J.; Liu, Y.; Lu, Y.; Wang, Q.; Li, G.; Zhang, R. [Corrigendum] Lycorine inhibits cell proliferation and migration by inhibiting ROCK1/cofilin-induced actin dynamics in HepG2 hepatoblastoma cells. *Oncol. Rep.* **2019**, *42*, 2856. [CrossRef] [PubMed]
234. Shen, J.; Ma, H.; Zhang, T.; Liu, H.; Yu, L.; Li, G.; Li, H.; Hu, M. Magnolol inhibits the growth of non-small cell lung cancer via inhibiting microtubule polymerization. *Cell. Physiol. Biochem.* **2017**, *42*, 1789–1801. [CrossRef] [PubMed]
235. Li, M.; Zhang, F.; Wang, X.A.; Wu, X.; Zhang, B.; Zhang, N.; Wu, W.; Wang, Z.; Weng, H.; Liu, S. Magnolol inhibits growth of gallbladder cancer cells through the p53 pathway. *Cancer Sci.* **2015**, *106*, 1341–1350. [CrossRef] [PubMed]
236. Kuan, L.-Y.; Chen, W.-L.; Chen, J.-H.; Hsu, F.-T.; Liu, T.-T.; Chen, W.-T.; Wang, K.-L.; Chen, W.-C.; Liu, Y.-C.; Wang, W.-S. Magnolol induces apoptosis and inhibits ERK-modulated metastatic potential in hepatocellular carcinoma cells. *Vivo* **2018**, *32*, 1361–1368. [CrossRef] [PubMed]
237. Hwang, E.-S.; Park, K.-K. Magnolol suppresses metastasis via inhibition of invasion, migration, and matrix metalloproteinase-2/-9 activities in PC-3 human prostate carcinoma cells. *Biosci. Biotechnol. Biochem.* **2010**, *74*, 961–967. [CrossRef]
238. Chen, Y.; Huang, K.; Ding, X.; Tang, H.; Xu, Z. Magnolol inhibits growth and induces apoptosis in esophagus cancer KYSE-150 cell lines via the MAP kinase pathway. *J. Thorac. Dis.* **2019**, *11*, 3030. [CrossRef]
239. Huang, H.; Wang, Q.; Du, T.; Lin, C.; Lai, Y.; Zhu, D.; Wu, W.; Ma, X.; Bai, S.; Li, Z. Matrine inhibits the progression of prostate cancer by promoting expression of GADD45B. *Prostate* **2018**, *78*, 327–335. [CrossRef]
240. Zhang, X.; Hou, G.; Liu, A.; Xu, H.; Guan, Y.; Wu, Y.; Deng, J.; Cao, X. Matrine inhibits the development and progression of ovarian cancer by repressing cancer associated phosphorylation signaling pathways. *Cell Death Dis.* **2019**, *10*, 1–17. [CrossRef]
241. Chang, C.; Liu, S.P.; Fang, C.H.; He, R.S.; Wang, Z.; Zhu, Y.Q.; Jiang, S.W. Effects of matrine on the proliferation of HT29 human colon cancer cells and its antitumor mechanism. *Oncol. Lett.* **2013**, *6*, 699–704. [CrossRef]
242. Lin, S.; Zhuang, J.; Zhu, L.; Jiang, Z. Matrine inhibits cell growth, migration, invasion and promotes autophagy in hepatocellular carcinoma by regulation of circ_0027345/miR-345-5p/HOXD3 axis. *Cancer Cell Int.* **2020**, *20*, 1–12. [CrossRef]
243. Pu, J.; Tang, X.; Zhuang, X.; Hu, Z.; He, K.; Wu, Y.; Dai, T. Matrine induces apoptosis via targeting CCR7 and enhances the effect of anticancer drugs in non-small cell lung cancer In Vitro. *Innate Immun.* **2018**, *24*, 394–399. [CrossRef] [PubMed]
244. Ha, T.K.; Jung, I.; Kim, M.E.; Bae, S.K.; Lee, J.S. Anti-cancer activity of myricetin against human papillary thyroid cancer cells involves mitochondrial dysfunction–mediated apoptosis. *Biomed. Pharmacother.* **2017**, *91*, 378–384. [CrossRef] [PubMed]
245. Sun, F.; Zheng, X.Y.; Ye, J.; Wu, T.T.; Wang, J.l.; Chen, W. Potential anticancer activity of myricetin in human T24 bladder cancer cells both In Vitro and In Vivo. *Nutr. Cancer* **2012**, *64*, 599–606. [CrossRef] [PubMed]

246. Kim, M.E.; Ha, T.K.; Yoon, J.H.; Lee, J.S. Myricetin induces cell death of human colon cancer cells via BAX/BCL2-dependent pathway. *Anticancer Res.* **2014**, *34*, 701–706.
247. Ye, C.; Zhang, C.; Huang, H.; Yang, B.; Xiao, G.; Kong, D.; Tian, Q.; Song, Q.; Song, Y.; Tan, H. The natural compound myricetin effectively represses the malignant progression of prostate cancer by inhibiting PIM1 and disrupting the PIM1/CXCR4 interaction. *Cell. Physiol. Biochem.* **2018**, *48*, 1230–1244. [CrossRef]
248. Knickle, A.; Fernando, W.; Greenshields, A.L.; Rupasinghe, H.V.; Hoskin, D.W. Myricetin-induced apoptosis of triple-negative breast cancer cells is mediated by the iron-dependent generation of reactive oxygen species from hydrogen peroxide. *Food Chem. Toxicol.* **2018**, *118*, 154–167. [CrossRef]
249. Kang, H.R.; Moon, J.Y.; Ediriweera, M.K.; Song, Y.W.; Cho, M.; Kasiviswanathan, D.; Cho, S.K. Dietary flavonoid myricetin inhibits invasion and migration of radioresistant lung cancer cells (A549-IR) by suppressing MMP-2 and MMP-9 expressions through inhibition of the FAK-ERK signaling pathway. *Food Sci. Nutr.* **2020**, *8*, 2059–2067. [CrossRef]
250. Subramani, R.; Gonzalez, E.; Arumugam, A.; Nandy, S.; Gonzalez, V.; Medel, J.; Camacho, F.; Ortega, A.; Bonkoungou, S.; Narayan, M. Nimbolide inhibits pancreatic cancer growth and metastasis through ROS-mediated apoptosis and inhibition of epithelial-to-mesenchymal transition. *Sci. Rep.* **2016**, *6*, 1–12. [CrossRef]
251. Gupta, S.C.; Prasad, S.; Sethumadhavan, D.R.; Nair, M.S.; Mo, Y.-Y.; Aggarwal, B.B. Nimbolide, a limonoid triterpene, inhibits growth of human colorectal cancer xenografts by suppressing the proinflammatory microenvironment. *Clin. Cancer Res.* **2013**, *19*, 4465–4476. [CrossRef]
252. Shin, S.-S.; Hwang, B.; Muhammad, K.; Gho, Y.; Song, J.-H.; Kim, W.-J.; Kim, G.; Moon, S.-K. Nimbolide represses the proliferation, migration, and invasion of bladder carcinoma cells via Chk2-mediated G2/M phase cell cycle arrest, altered signaling pathways, and reduced transcription factors-associated MMP-9 expression. *Evid. Based Complement. Alternat. Med.* **2019**, *2019*, 3753587. [CrossRef]
253. Tian, X.; Liu, M.; Huang, X.; Zhu, Q.; Liu, W.; Chen, W.; Zou, Y.; Cai, Y.; Huang, S.; Chen, A. Noscapine induces apoptosis in human colon cancer cells by regulating mitochondrial damage and warburg effect via PTEN/PI3K/mTOR signaling pathway. *Onco Targets Ther.* **2020**, *13*, 5419. [CrossRef]
254. Quisbert-Valenzuela, E.O.; Calaf, G.M. Apoptotic effect of noscapine in breast cancer cell lines. *Int. J. Oncol.* **2016**, *48*, 2666–2674. [CrossRef] [PubMed]
255. Jackson, T.; Chougule, M.B.; Ichite, N.; Patlolla, R.R.; Singh, M. Antitumor activity of noscapine in human non-small cell lung cancer xenograft model. *Cancer Chemother. Pharmacol.* **2008**, *63*, 117–126. [CrossRef] [PubMed]
256. Barken, I.; Geller, J.; Rogosnitzky, M. Prophylactic noscapine therapy inhibits human prostate cancer progression and metastasis in a mouse model. *Anticancer Res.* **2010**, *30*, 399–401. [PubMed]
257. Yao, Z.; Xie, F.; Li, M.; Liang, Z.; Xu, W.; Yang, J.; Liu, C.; Li, H.; Zhou, H.; Qu, L.-H. Oridonin induces autophagy via inhibition of glucose metabolism in p53-mutated colorectal cancer cells. *Cell Death Dis.* **2017**, *8*, e2633. [CrossRef] [PubMed]
258. Li, X.; Chen, W.; Liu, K.; Zhang, S.; Yang, R.; Liu, K.; Li, D.; Huang, Y. Oridonin sensitizes hepatocellular carcinoma to the anticancer effect of sorafenib by targeting the Akt pathway. *Cancer Manag. Res.* **2020**, *12*, 8081. [CrossRef]
259. Wang, Y.; Zhu, Z. Oridonin inhibits metastasis of human ovarian cancer cells by suppressing the mTOR pathway. *Arch. Med. Sci.* **2019**, *15*, 1017. [CrossRef]
260. Che, X.; Zhan, J.; Zhao, F.; Zhong, Z.; Chen, M.; Han, R.; Wang, Y. Oridonin Promotes Apoptosis and Restrains the Viability and Migration of Bladder Cancer by Impeding TRPM7 Expression via the ERK and AKT Signaling Pathways. *Biomed Res. Int.* **2021**, *2021*, 4340950. [CrossRef]
261. Song, M.; Liu, X.; Liu, K.; Zhao, R.; Huang, H.; Shi, Y.; Zhang, M.; Zhou, S.; Xie, H.; Chen, H. Targeting AKT with oridonin inhibits growth of esophageal squamous cell carcinoma In Vitro and patient-derived xenografts In Vivo. *Mol. Cancer Ther.* **2018**, *17*, 1540–1553. [CrossRef]
262. Wang, S.; Zhong, Z.; Wan, J.; Tan, W.; Wu, G.; Chen, M.; Wang, Y. Oridonin induces apoptosis, inhibits migration and invasion on highly-metastatic human breast cancer cells. *Am. J. Chin. Med.* **2013**, *41*, 177–196. [CrossRef]
263. Lu, Y.; Sun, Y.; Zhu, J.; Yu, L.; Jiang, X.; Zhang, J.; Dong, X.; Ma, B.; Zhang, Q. Oridonin exerts anticancer effect on osteosarcoma by activating PPAR-γ and inhibiting Nrf2 pathway. *Cell Death Dis.* **2018**, *9*, 1–16. [CrossRef] [PubMed]
264. Zhou, Y.J.; Guo, Y.J.; Yang, X.L.; Ou, Z.L. Anti-cervical cancer role of matrine, oxymatrine and sophora flavescens alkaloid gels and its mechanism. *J. Cancer* **2018**, *9*, 1357. [CrossRef] [PubMed]
265. Guo, L.; Yang, T. Oxymatrine inhibits the proliferation and invasion of breast cancer cells via the PI3K pathway. *Cancer Manag. Res.* **2019**, *11*, 10499. [CrossRef] [PubMed]
266. Ling, Q.; Xu, X.; Wei, X.; Wang, W.; Zhou, B.; Wang, B.; Zheng, S. Oxymatrine induces human pancreatic cancer PANC-1 cells apoptosis via regulating expression of Bcl-2 and IAP families, and releasing of cytochrome c. *J. Exp. Clin. Cancer Res.* **2011**, *30*, 66. [CrossRef]
267. Wu, C.; Huang, W.; Guo, Y.; Xia, P.; Sun, X.; Pan, X.; Hu, W. Oxymatrine inhibits the proliferation of prostate cancer cells In Vitro and In Vivo. *Mol. Med. Rep.* **2015**, *11*, 4129–4134. [CrossRef]
268. Zhao, X.; Huang, L.; Xu, W.; Chen, X.; Shen, Y.; Zeng, W.; Chen, X. Physapubescin B inhibits tumorgenesis and circumvents taxol resistance of ovarian cancer cells through STAT3 signaling. *Oncotarget* **2017**, *8*, 70130. [CrossRef]
269. Chen, L.; Xia, G.; Qiu, F.; Wu, C.; Denmon, A.P.; Zi, X. Physapubescin selectively induces apoptosis in VHL-null renal cell carcinoma cells through down-regulation of HIF-2α and inhibits tumor growth. *Sci. Rep.* **2016**, *6*, 1–12. [CrossRef]

270. Jaudan, A.; Sharma, S.; Malek, S.N.A.; Dixit, A. Induction of apoptosis by pinostrobin in human cervical cancer cells: Possible mechanism of action. *PLoS ONE* **2018**, *13*, e0191523. [CrossRef]
271. Jones, A.A.; Gehler, S. Acacetin and pinostrobin inhibit malignant breast epithelial cell adhesion and focal adhesion formation to attenuate cell migration. *Integr. Cancer Ther.* **2020**, *19*, 1534735420918945. [CrossRef]
272. Roman, W.A.; Gomes, D.B.; Zanchet, B.; Schönell, A.P.; Diel, K.A.; Banzato, T.P.; Ruiz, A.L.; Carvalho, J.E.; Neppel, A.; Barison, A. Antiproliferative effects of pinostrobin and 5, 6-dehydrokavain isolated from leaves of Alpinia zerumbet. *Rev. Bras. Farmacogn.* **2017**, *27*, 592–598.
273. Haddad, A.; Venkateswaran, V.; Viswanathan, L.; Teahan, S.; Fleshner, N.; Klotz, L. Novel antiproliferative flavonoids induce cell cycle arrest in human prostate cancer cell lines. *Prostate Cancer Prostatic Dis.* **2006**, *9*, 68–76. [CrossRef] [PubMed]
274. de Almeida, G.C.; Oliveira, L.F.; Predes, D.; Fokoue, H.H.; Kuster, R.M.; Oliveira, F.L.; Mendes, F.A.; Abreu, J.G. Piperine suppresses the Wnt/β-catenin pathway and has anti-cancer effects on colorectal cancer cells. *Sci. Rep.* **2020**, *10*, 1–12. [CrossRef] [PubMed]
275. Lin, Y.; Xu, J.; Liao, H.; Li, L.; Pan, L. Piperine induces apoptosis of lung cancer A549 cells via p53-dependent mitochondrial signaling pathway. *Tumor Biol.* **2014**, *35*, 3305–3310. [CrossRef] [PubMed]
276. Lai, L.H.; Fu, Q.H.; Liu, Y.; Jiang, K.; Guo, Q.M.; Chen, Q.Y.; Yan, B.; Wang, Q.Q.; Shen, J.G. Piperine suppresses tumor growth and metastasis In Vitro and In Vivo in a 4T1 murine breast cancer model. *Acta Pharmacol. Sin.* **2012**, *33*, 523–530. [CrossRef]
277. Ouyang, D.-Y.; Zeng, L.H.; Pan, H.; Xu, L.H.; Wang, Y.; Liu, K.P.; He, X.H. Piperine inhibits the proliferation of human prostate cancer cells via induction of cell cycle arrest and autophagy. *Food Chem. Toxicol.* **2013**, *60*, 424–430. [CrossRef]
278. Zhang, C.; He, L.-J.; Zhu, Y.-B.; Fan, Q.-Z.; Miao, D.-D.; Zhang, S.-P.; Zhao, W.-Y.; Liu, X.-P. Piperlongumine inhibits Akt phosphorylation to reverse resistance to cisplatin in human non-small cell lung cancer cells via ROS regulation. *Front. Pharmacol.* **2019**, *10*, 1178. [CrossRef]
279. Zhang, D.F.; Yang, Z.C.; Chen, J.Q.; Jin, X.X.; Chen, X.J.; Shi, H.Y.; Liu, Z.G.; Wang, M.S.; Liang, G.; Zheng, X.H. Piperlongumine inhibits migration and proliferation of castration-resistant prostate cancer cells via triggering persistent DNA damage. *BMC Complement. Med. Ther.* **2021**, *21*, 1–15. [CrossRef]
280. Machado, F.D.S.; Munari, F.M.; Scariot, F.J.; Echeverrigaray, S.; Aguzzoli, C.; Pich, C.T.; Kato, M.J.; Yamaguchi, L.; Moura, S.; Henriques, J.A.P. Piperlongumine induces apoptosis in colorectal cancer HCT 116 cells independent of Bax, p21 and p53 status. *Anticancer Res.* **2018**, *38*, 6231–6236. [CrossRef]
281. Zhang, X.; Yang, C.; Rao, X.; Xiong, J. Plumbagin shows anti-cancer activity in human breast cancer cells by the upregulation of p53 and p21 and suppression of G1 cell cycle regulators. *Eur. J. Gynaecol. Oncol.* **2016**, *37*, 30–35.
282. Eldhose, B.; GUNAwAN, M.; Rahman, M.; Latha, M.S.; Notario, V. Plumbagin reduces human colon cancer cell survival by inducing cell cycle arrest and mitochondria-mediated apoptosis. *Int. J. Oncol.* **2014**, *45*, 1913–1920. [CrossRef]
283. Li, T.; Lv, M.; Chen, X.; Yu, Y.; Zang, G.; Tang, Z. Plumbagin inhibits proliferation and induces apoptosis of hepatocellular carcinoma by downregulating the expression of SIVA. *Drug Des. Devel. Ther.* **2019**, *13*, 1289. [CrossRef] [PubMed]
284. Huang, H.; Xie, H.; Pan, Y.; Zheng, K.; Xia, Y.; Chen, W. Plumbagin triggers ER stress-mediated apoptosis in prostate cancer cells via induction of ROS. *Cell. Physiol. Biochem.* **2018**, *45*, 267–280. [CrossRef] [PubMed]
285. Tripathi, S.K.; Rengasamy, K.R.; Biswal, B.K. Plumbagin engenders apoptosis in lung cancer cells via caspase-9 activation and targeting mitochondrial-mediated ROS induction. *Arch. Pharm. Res.* **2020**, *43*, 242–256. [CrossRef] [PubMed]
286. Cao, Y.-Y.; Yu, J.; Liu, T.-T.; Yang, K.-X.; Yang, L.-Y.; Chen, Q.; Shi, F.; Hao, J.-J.; Cai, Y.; Wang, M.-R. Plumbagin inhibits the proliferation and survival of esophageal cancer cells by blocking STAT3-PLK1-AKT signaling. *Cell Death Dis.* **2018**, *9*, 1–13. [CrossRef] [PubMed]
287. Yan, C.-H.; Li, F.; Ma, Y.-C. Plumbagin shows anticancer activity in human osteosarcoma (MG-63) cells via the inhibition of S-Phase checkpoints and down-regulation of c-myc. *Int. J. Clin. Exp. Med.* **2015**, *8*, 14432. [PubMed]
288. Jaiswal, A.; Sabarwal, A.; Mishra, J.P.N.; Singh, R.P. Plumbagin induces ROS-mediated apoptosis and cell cycle arrest and inhibits EMT in human cervical carcinoma cells. *RSC Adv.* **2018**, *8*, 32022–32037. [CrossRef]
289. Seo, H.W.; Park, J.-H.; Lee, J.Y.; Park, H.-J.; Kim, J.-K. Pristimerin, a Naturally Occurring Triterpenoid, Exerts Potent Anticancer Effect in Colon Cancer Cells. *Biomed. Sci.* **2018**, *24*, 15–22. [CrossRef]
290. Wu, H.; Li, L.; Ai, Z.; Yin, J.; Chen, L. Pristimerin induces apoptosis of oral squamous cell carcinoma cells via G1 phase arrest and MAPK/Erk1/2 and Akt signaling inhibition. *Oncol. Lett.* **2019**, *17*, 3017–3025. [CrossRef]
291. Lee, S.-O.; Kim, J.-S.; Lee, M.-S.; Lee, H.-J. Anti-cancer effect of pristimerin by inhibition of HIF-1α involves the SPHK-1 pathway in hypoxic prostate cancer cells. *BMC Cancer* **2016**, *16*, 1–10. [CrossRef]
292. Li, J.; Guo, Q.; Lei, X.; Zhang, L.; Su, C.; Liu, Y.; Zhou, W.; Chen, H.; Wang, H.; Wang, F. Pristimerin induces apoptosis and inhibits proliferation, migration in H1299 Lung Cancer Cells. *J. Cancer* **2020**, *11*, 6348. [CrossRef]
293. Deeb, D.; Gao, X.; Liu, Y.B.; Pindolia, K.; Gautam, S.C. Pristimerin, a quinonemethide triterpenoid, induces apoptosis in pancreatic cancer cells through the inhibition of pro-survival Akt/NF-κB/mTOR signaling proteins and anti-apoptotic Bcl-2. *Int. J. Oncol.* **2014**, *44*, 1707–1715. [CrossRef] [PubMed]
294. Pei, H.L.; Mu, D.M.; Zhang, B. Anticancer activity of pterostilbene in human ovarian cancer cell lines. *Med. Sci. Monit. Basic Res.* **2017**, *23*, 3192. [CrossRef] [PubMed]
295. Ma, Z.; Yang, Y.; Di, S.; Feng, X.; Liu, D.; Jiang, S.; Hu, W.; Qin, Z.; Li, Y.; Lv, J. Pterostilbene exerts anticancer activity on non-small-cell lung cancer via activating endoplasmic reticulum stress. *Sci. Rep.* **2017**, *7*, 1–14. [CrossRef] [PubMed]

296. Wakimoto, R.; Ono, M.; Takeshima, M.; Higuchi, T.; Nakano, S. Differential anticancer activity of pterostilbene against three subtypes of human breast cancer cells. *Anticancer Res.* **2017**, *37*, 6153–6159.
297. Zhang, Y.; Li, Y.; Sun, C.; Chen, X.; Han, L.; Wang, T.; Liu, J.; Chen, X.; Zhao, D. Effect of Pterostilbene, a Natural Derivative of Resveratrol, in the Treatment of Colorectal Cancer through Top1/Tdp1-Mediated DNA Repair Pathway. *Cancers* **2021**, *13*, 4002. [CrossRef]
298. Yu, Z.; Li, W. Induction of apoptosis by puerarin in colon cancer HT-29 cells. *Cancer Lett.* **2006**, *238*, 53–60. [CrossRef]
299. Li, J.; Xiong, C.; Xu, P.; Luo, Q.; Zhang, R. Puerarin induces apoptosis in prostate cancer cells via inactivation of the Keap1/Nrf2/ARE signaling pathway. *Bioengineered* **2021**, *12*, 402–413. [CrossRef]
300. Hu, Y.; Li, X.; Lin, L.; Liang, S.; Yan, J. Puerarin inhibits non-small cell lung cancer cell growth via the induction of apoptosis. *Oncol. Rep.* **2018**, *39*, 1731–1738. [CrossRef]
301. Zhang, W.-G.; Yin, X.-C.; Liu, X.-F.; Meng, K.-W.; Tang, K.; Huang, F.-L.; Xu, G.; Gao, J. Puerarin induces hepatocellular carcinoma cell apoptosis modulated by MAPK signaling pathways in a dose-dependent manner. *Anticancer Res.* **2017**, *37*, 4425–4431.
302. Yang, J.-A.; Li, J.-Q.; Shao, L.-M.; Yang, Q.; Liu, B.-H.; Wu, T.-F.; Wu, P.; Yi, W.; Chen, Q.-X. Puerarin inhibits proliferation and induces apoptosis in human glioblastoma cell lines. *Int. J. Clin. Exp. Med.* **2015**, *8*, 10132.
303. Hong, Y.; Lee, J.; Moon, H.; Ryu, C.H.; Seok, J.; Jung, Y.; Ryu, J.; Baek, S.J. Quercetin Induces Anticancer Activity by Upregulating Pro-NAG-1/GDF15 in Differentiated Thyroid Cancer Cells. *Cancers* **2021**, *13*, 3022. [CrossRef] [PubMed]
304. Mohammed, H.A.; Sulaiman, G.M.; Anwar, S.S.; Tawfeeq, A.T.; Khan, R.A.; Mohammed, S.A.; Al-Omar, M.S.; Alsharidah, M.; Rugaie, O.A.; Al-Amiery, A.A. Quercetin against MCF7 and CAL51 breast cancer cell lines: Apoptosis, gene expression and cytotoxicity of nano-quercetin. *Nanomedicine* **2021**, *16*, 1937–1961. [CrossRef] [PubMed]
305. Hisaka, T.; Sakai, H.; Sato, T.; Goto, Y.; Nomura, Y.; Fukutomi, S.; Fujita, F.; Mizobe, T.; Nakashima, O.; Tanigawa, M. Quercetin suppresses proliferation of liver cancer cell lines In Vitro. *Anticancer Res.* **2020**, *40*, 4695–4700. [CrossRef] [PubMed]
306. Nair, H.K.; Rao, K.V.; Aalinkeel, R.; Mahajan, S.; Chawda, R.; Schwartz, S.A. Inhibition of prostate cancer cell colony formation by the flavonoid quercetin correlates with modulation of specific regulatory genes. *Clin. Vaccine Immunol.* **2004**, *11*, 63–69. [CrossRef] [PubMed]
307. Youn, H.; Jeong, J.-C.; Jeong, Y.S.; Kim, E.-J.; Um, S.-J. Quercetin potentiates apoptosis by inhibiting nuclear factor-kappaB signaling in H460 lung cancer cells. *Biol. Pharm. Bull.* **2013**, *36*, 944–951. [CrossRef] [PubMed]
308. Zeng, Y.-H.; Zhou, L.-Y.; Chen, Q.-Z.; Li, Y.; Shao, Y.; Ren, W.-Y.; Liao, Y.-P.; Wang, H.; Zhu, J.-H.; Huang, M. Resveratrol inactivates PI3K/Akt signaling through upregulating BMP7 in human colon cancer cells. *Oncol. Rep.* **2017**, *38*, 456–464. [CrossRef]
309. Miksits, M.; Wlcek, K.; Svoboda, M.; Kunert, O.; Haslinger, E.; Thalhammer, T.; Szekeres, T.; Jäger, W. Antitumor activity of resveratrol and its sulfated metabolites against human breast cancer cells. *Planta Med.* **2009**, *75*, 1227–1230. [CrossRef]
310. Zhong, L.; Zhang, Y.; Wu, M.; Liu, Y.; Zhang, P.; Chen, X.; Kong, Q.; Liu, J.; Li, H. Resveratrol and STAT inhibitor enhance autophagy in ovarian cancer cells. *Cell Death Discov.* **2016**, *2*, 1–8. [CrossRef]
311. Cheng, L.; Yan, B.; Chen, K.; Jiang, Z.; Zhou, C.; Cao, J.; Qian, W.; Li, J.; Sun, L.; Ma, J. Resveratrol-induced downregulation of NAF-1 enhances the sensitivity of pancreatic cancer cells to gemcitabine via the ROS/Nrf2 signaling pathways. *Oxid. Med. Cell. Longev.* **2018**, *2018*. [CrossRef]
312. Wu, X.; Xu, Y.; Zhu, B.; Liu, Q.; Yao, Q.; Zhao, G. Resveratrol induces apoptosis in SGC-7901 gastric cancer cells. *Oncol. Lett.* **2018**, *16*, 2949–2956. [CrossRef]
313. Yousef, M.; Vlachogiannis, I.A.; Tsiani, E. Effects of resveratrol against lung cancer: In vitro and In Vivo studies. *Nutrients* **2017**, *9*, 1231. [CrossRef] [PubMed]
314. Chao, S.-C.; Chen, Y.-J.; Huang, K.-H.; Kuo, K.-L.; Yang, T.-H.; Huang, K.-Y.; Wang, C.-C.; Tang, C.-H.; Yang, R.-S.; Liu, S.-H. Induction of sirtuin-1 signaling by resveratrol induces human chondrosarcoma cell apoptosis and exhibits antitumor activity. *Sci. Rep.* **2017**, *7*, 1–11. [CrossRef] [PubMed]
315. Jayameena, P.; Sivakumari, K.; Ashok, K.; Rajesh, S. Rutin: A potential anticancer drug against human colon cancer (HCT116) cells. *Int. J. Biol. Pharm. Allied Sci.* **2018**, *7*, 1731–1745.
316. Pinzaru, I.; Chioibas, R.; Marcovici, I.; Coricovac, D.; Susan, R.; Predut, D.; Georgescu, D.; Dehelean, C. Rutin Exerts Cytotoxic and Senescence-Inducing Properties in Human Melanoma Cells. *Toxics* **2021**, *9*, 226. [CrossRef] [PubMed]
317. Elsayed, H.E.; Ebrahim, H.Y.; Mohyeldin, M.M.; Siddique, A.B.; Kamal, A.M.; Haggag, E.G.; El Sayed, K.A. Rutin as a novel c-Met inhibitory lead for the control of triple negative breast malignancies. *Nutr. Cancer* **2017**, *69*, 1256–1271. [CrossRef]
318. Zhang, Y.; Zhao, Y.; Guo, J.; Cui, H.; Liu, S. Anticancer activity of safranal against colon carcinoma is due to induction of apoptosis and G2/M cell cycle arrest mediated by suppression of mTOR/PI3K/Akt pathway. *JBU ON* **2018**, *23*, 574–578.
319. Chaiboonchoe, A.; Khraiwesh, B.; Murali, C.; Baig, B.; El-Awady, R.; Tarazi, H.; Alzahmi, A.; Nelson, D.R.; Greish, Y.E.; Ramadan, W. Safranal induces DNA double-strand breakage and ER-stress-mediated cell death in hepatocellular carcinoma cells. *Sci. Rep.* **2018**, *8*, 1–15.
320. Jiang, X.; Li, Y.; Feng, J.L.; Nik Nabil, W.N.; Wu, R.; Lu, Y.; Liu, H.; Xi, Z.C.; Xu, H.X. Safrana l prevents prostate cancer recurrence by blocking the Re-activation of quiescent cancer cells via downregulation of S-phase kinase-associated protein 2. *Front. Cell Dev. Biol.* **2020**, *8*, 1553. [CrossRef]
321. Chryssanthi, D.G.; Lamari, F.N.; Iatrou, G.; Pylara, A.; Karamanos, N.K.; Cordopatis, P. Inhibition of breast cancer cell proliferation by style constituents of different Crocus species. *Anticancer Res.* **2007**, *27*, 357–362.

322. Sha, L.; Lv, Z.; Liu, Y.; Zhang, Y.; Sui, X.; Wang, T.; Zhang, H. Shikonin inhibits the Warburg effect, cell proliferation, invasion and migration by downregulating PFKFB2 expression in lung cancer. *Mol. Med. Rep.* **2021**, *24*, 1–10. [CrossRef]
323. Chandimali, N.; Sun, H.-N.; Kong, L.-Z.; Zhen, X.; Liu, R.; Kwon, T.; Lee, D.-S. Shikonin-induced apoptosis of colon cancer cells is reduced by peroxiredoxin V expression. *Anticancer Res.* **2019**, *39*, 6115–6123. [CrossRef] [PubMed]
324. Markowitsch, S.D.; Juetter, K.M.; Schupp, P.; Hauschulte, K.; Vakhrusheva, O.; Slade, K.S.; Thomas, A.; Tsaur, I.; Cinatl, J.; Michaelis, M. Shikonin Reduces Growth of Docetaxel-Resistant Prostate Cancer Cells Mainly through Necroptosis. *Cancers* **2021**, *13*, 882. [CrossRef] [PubMed]
325. Liu, T.; Li, S.; Wu, L.; Yu, Q.; Li, J.; Feng, J.; Zhang, J.; Chen, J.; Zhou, Y.; Ji, J. Experimental study of hepatocellular carcinoma treatment by shikonin through regulating PKM2. *J. Hepatocell. Carcinoma* **2020**, *7*, 19. [CrossRef] [PubMed]
326. Shilnikova, K.; Piao, M.J.; Kang, K.A.; Ryu, Y.S.; Park, J.E.; Hyun, Y.J.; Zhen, A.X.; Jeong, Y.J.; Jung, U.; Kim, I.G. Shikonin induces mitochondria-mediated apoptosis and attenuates epithelial-mesenchymal transition in cisplatin-resistant human ovarian cancer cells. *Oncol. Lett.* **2018**, *15*, 5417–5424. [CrossRef]
327. Lee, J.H.; Han, S.H.; Kim, Y.M.; Kim, S.H.; Yoo, E.S.; Woo, J.S.; Jung, G.H.; Jung, S.H.; Kim, B.S.; Jung, J.Y. Shikonin inhibits proliferation of melanoma cells by MAPK pathway-mediated induction of apoptosis. *Biosci. Rep.* **2021**, *41*, BSR20203834. [CrossRef]
328. Thonsri, U.; Seubwai, W.; Waraasawapati, S.; Wongkham, S.; Boonmars, T.; Cha'on, U.; Wongkham, C. Antitumor Effect of Shikonin, a PKM2 Inhibitor, in Cholangiocarcinoma Cell Lines. *Anticancer Res.* **2020**, *40*, 5115–5124. [CrossRef]
329. Hou, Y.; Guo, T.; Wu, C.; He, X.; Zhao, M. Effect of shikonin on human breast cancer cells proliferation and apoptosis In Vitro. *Yakugaku Zasshi* **2006**, *126*, 1383–1386. [CrossRef]
330. Bawadood, A.S.; Al-Abbasi, F.A.; Anwar, F.; El-Halawany, A.M.; Al-Abd, A.M. 6-Shogaol suppresses the growth of breast cancer cells by inducing apoptosis and suppressing autophagy via targeting notch signaling pathway. *Biomed. Pharmacother.* **2020**, *128*, 110302. [CrossRef]
331. Saha, A.; Blando, J.; Silver, E.; Beltran, L.; Sessler, J.; DiGiovanni, J. 6-Shogaol from dried ginger inhibits growth of prostate cancer cells both In Vitro and In Vivo through inhibition of STAT3 and NF-κB signaling. *Cancer Prev. Res.* **2014**, *7*, 627–638. [CrossRef]
332. Hsu, Y.-L.; Hung, J.-Y.; Tsai, Y.-M.; Tsai, E.-M.; Huang, M.-S.; Hou, M.-F.; Kuo, P.-L. 6-shogaol, an active constituent of dietary ginger, impairs cancer development and lung metastasis by inhibiting the secretion of CC-chemokine ligand 2 (CCL2) in tumor-associated dendritic cells. *J. Agric. Food Chem.* **2015**, *63*, 1730–1738. [CrossRef]
333. Liu, Q.; Peng, Y.-B.; Qi, L.-W.; Cheng, X.-L.; Xu, X.J.; Liu, L.-L.; Liu, E.-H.; Li, P. The cytotoxicity mechanism of 6-shogaol-treated HeLa human cervical cancer cells revealed by label-free shotgun proteomics and bioinformatics analysis. *Evid. Based Complement. Alternat. Med.* **2012**, *2012*, 278652. [CrossRef] [PubMed]
334. Kil, W.H.; Kim, S.M.; Lee, J.E.; Park, K.S.; Nam, S.J. Anticancer effect of silibinin on the xenograft model using MDA-MB-468 breast cancer cells. *Ann. Surg. Treat. Res.* **2014**, *87*, 167–173. [CrossRef] [PubMed]
335. Hou, X.; Du, H.; Quan, X.; Shi, L.; Zhang, Q.; Wu, Y.; Liu, Y.; Xiao, J.; Li, Y.; Lu, L. Silibinin inhibits NSCLC metastasis by targeting the EGFR/LOX pathway. *Front. Pharmacol.* **2018**, *9*, 21. [CrossRef] [PubMed]
336. Cho, H.J.; Suh, D.S.; Moon, S.H.; Song, Y.J.; Yoon, M.S.; Park, D.Y.; Choi, K.U.; Kim, Y.K.; Kim, K.H. Silibinin inhibits tumor growth through downregulation of extracellular signal-regulated kinase and Akt In Vitro and In Vivo in human ovarian cancer cells. *J. Agric. Food Chem.* **2013**, *61*, 4089–4096. [CrossRef]
337. Deep, G.; Singh, R.; Agarwal, C.; Kroll, D.; Agarwal, R. Silymarin and silibinin cause G1 and G2–M cell cycle arrest via distinct circuitries in human prostate cancer PC3 cells: A comparison of flavanone silibinin with flavanolignan mixture silymarin. *Oncogene* **2006**, *25*, 1053–1069. [CrossRef]
338. Sati, J.; Mohanty, B.P.; Garg, M.L.; Koul, A. Pro-oxidant role of silibinin in DMBA/TPA induced skin cancer: 1H NMR metabolomic and biochemical study. *PLoS ONE* **2016**, *11*, e0158955. [CrossRef]
339. Sameri, S.; Mohammadi, C.; Mehrabani, M.; Najafi, R. Targeting the hallmarks of cancer: The effects of silibinin on proliferation, cell death, angiogenesis, and migration in colorectal cancer. *BMC Complement. Med. Ther.* **2021**, *21*, 1–9. [CrossRef]
340. Wang, Y.-X.; Cai, H.; Jiang, G.; Zhou, T.-B.; Wu, H. Silibinin inhibits proliferation, induces apoptosis and causes cell cycle arrest in human gastric cancer MGC803 cells via STAT3 pathway inhibition. *Asian Pac. J. Cancer Prev.* **2014**, *15*, 6791–6798. [CrossRef]
341. Kim, S.H.; Choo, G.S.; Yoo, E.S.; Woo, J.S.; Han, S.H.; Lee, J.H.; Jung, J.Y. Silymarin induces inhibition of growth and apoptosis through modulation of the MAPK signaling pathway in AGS human gastric cancer cells. *Oncol. Rep.* **2019**, *42*, 1904–1914. [CrossRef]
342. Kim, S.-H.; Choo, G.-S.; Yoo, E.-S.; Woo, J.-S.; Lee, J.-H.; Han, S.-H.; Jung, S.-H.; Kim, H.-J.; Jung, J.-Y. Silymarin inhibits proliferation of human breast cancer cells via regulation of the MAPK signaling pathway and induction of apoptosis. *Oncol. Lett.* **2021**, *21*, 1–10. [CrossRef]
343. Wu, Y.-F.; Fu, S.-L.; Kao, C.-H.; Yang, C.-W.; Lin, C.-H.; Hsu, M.-T.; Tsai, T.-F. Chemopreventive effect of silymarin on liver pathology in HBV X protein transgenic mice. *Cancer Res.* **2008**, *68*, 2033–2042. [CrossRef]
344. Fu, R.; Wang, X.; Hu, Y.; Du, H.; Dong, B.; Ao, S.; Zhang, L.; Sun, Z.; Zhang, L.; Lv, G. Solamargine inhibits gastric cancer progression by regulating the expression of lncNEAT1_2 via the MAPK signaling pathway. *Int. J. Oncol.* **2019**, *54*, 1545–1554. [CrossRef]

345. Al Sinani, S.S.; Eltayeb, E.A.; Coomber, B.L.; Adham, S.A. Solamargine triggers cellular necrosis selectively in different types of human melanoma cancer cells through extrinsic lysosomal mitochondrial death pathway. *Cancer Cell Int.* **2016**, *16*, 1–12. [CrossRef]
346. Liu, J.; Wang, Z.; Xu, C.; Qi, Y.; Zhang, Q. Solamargine inhibits proliferation and promotes apoptosis of CM-319 human chordoma cells through suppression of notch pathway. *Transl. Cancer Res.* **2019**, *8*, 509–519. [CrossRef]
347. Fekry, M.I.; Ezzat, S.M.; Salama, M.M.; Alshehri, O.Y.; Al-Abd, A.M. Bioactive glycoalkaloides isolated from Solanum melongena fruit peels with potential anticancer properties against hepatocellular carcinoma cells. *Sci. Rep.* **2019**, *9*, 1–11. [CrossRef]
348. Xiang, S.; Zhang, Q.; Tang, Q.; Zheng, F.; Wu, J.; Yang, L.; Hann, S.S. Activation of AMPKα mediates additive effects of solamargine and metformin on suppressing MUC1 expression in castration-resistant prostate cancer cells. *Sci. Rep.* **2016**, *6*, 1–14. [CrossRef]
349. Wang, M.; Shu, Z.-J.; Wang, Y.; Peng, W. Stachydrine hydrochloride inhibits proliferation and induces apoptosis of breast cancer cells via inhibition of Akt and ERK pathways. *Am. J. Transl. Res.* **2017**, *9*, 1834.
350. Rathee, P.; Rathee, D.; Rathee, D.; Rathee, S. In vitro anticancer activity of stachydrine isolated from Capparis decidua on prostate cancer cell lines. *Nat. Prod. Res.* **2012**, *26*, 1737–1740. [CrossRef]
351. Wang, Y.; Shi, L.-Y.; Qi, W.-H.; Yang, J.; Qi, Y. Anticancer activity of sugiol against ovarian cancer cell line SKOV3 involves mitochondrial apoptosis, cell cycle arrest and blocking of the RAF/MEK/ERK signalling pathway. *Arch. Med. Sci.* **2020**, *16*, 428. [CrossRef]
352. Jung, S.-N.; Shin, D.-S.; Kim, H.-N.; Jeon, Y.J.; Yun, J.; Lee, Y.-J.; Kang, J.S.; Han, D.C.; Kwon, B.-M. Sugiol inhibits STAT3 activity via regulation of transketolase and ROS-mediated ERK activation in DU145 prostate carcinoma cells. *Biochem. Pharmacol.* **2015**, *97*, 38–50. [CrossRef]
353. Hao, C.; Zhang, X.; Zhang, H.; Shang, H.; Bao, J.; Wang, H.; Li, Z. Sugiol (12-hydroxyabieta-8, 11, 13-trien-7-one) targets hu-man pancreatic carcinoma cells (Mia-PaCa2) by inducing ap-optosis, G2/M cell cycle arrest, ROS production and inhibi-tion of cancer cell migration. *J. BUON* **2018**, *23*, 205–210. [PubMed]
354. Zhao, H.; Zhang, X. Sugiol suppresses the growth, migration, and invasion of human endometrial cancer cells via induction of apoptosis and autophagy. *3 Biotech* **2021**, *11*, 1–9. [CrossRef] [PubMed]
355. Lee, C.-Y.; Sher, H.-F.; Chen, H.-W.; Liu, C.-C.; Chen, C.-H.; Lin, C.-S.; Yang, P.-C.; Tsay, H.-S.; Chen, J.J. Anticancer effects of tanshinone I in human non-small cell lung cancer. *Mol. Cancer Ther.* **2008**, *7*, 3527–3538. [CrossRef] [PubMed]
356. Zhang, Y.; Guo, S.; Fang, J.; Peng, B.; Zhang, Y.; Cao, T. Tanshinone IIA inhibits cell proliferation and tumor growth by downregulating STAT3 in human gastric cancer. *Exp. Ther. Med.* **2018**, *16*, 2931–2937. [CrossRef]
357. Li, G.; Shan, C.; Liu, L.; Zhou, T.; Zhou, J.; Hu, X.; Chen, Y.; Cui, H.; Gao, N. Tanshinone IIA inhibits HIF-1α and VEGF expression in breast cancer cells via mTOR/p70S6K/RPS6/4E-BP1 signaling pathway. *PLoS ONE* **2015**, *10*, e0117440. [CrossRef]
358. Zhou, J.; Jiang, Y.-Y.; Wang, X.-X.; Wang, H.-P.; Chen, H.; Wu, Y.-C.; Wang, L.; Pu, X.; Yue, G.-Z.; Zhang, L. Tanshinone IIA suppresses ovarian cancer growth through inhibiting malignant properties and angiogenesis. *Ann. Transl. Med.* **2020**, *8*, 1295. [CrossRef]
359. Chiu, S.-C.; Huang, S.-Y.; Chang, S.-F.; Chen, S.-P.; Chen, C.-C.; Lin, T.-H.; Liu, H.-H.; Tsai, T.-H.; Lee, S.-S.; Pang, C.-Y. Potential therapeutic roles of tanshinone IIA in human bladder cancer cells. *Int. J. Mol. Sci.* **2014**, *15*, 15622–15637. [CrossRef]
360. Li, M.; Wang, G.; Zhang, R.; Duan, S.; Chen, J. Tanshinone IIA inhibits proliferation and activates apoptosis in C4-1 cervical carcinoma cells In Vitro. *Biotechnol. Biotechnol. Equip.* **2019**, *33*, 1599–1607. [CrossRef]
361. Park, M.H.; Hong, J.E.; Park, E.S.; Yoon, H.S.; Seo, D.W.; Hyun, B.K.; Han, S.-B.; Ham, Y.W.; Hwang, B.Y.; Hong, J.T. Anticancer effect of tectochrysin in colon cancer cell via suppression of NF-kappaB activity and enhancement of death receptor expression. *Mol. Cancer* **2015**, *14*, 1–12. [CrossRef]
362. Wang, Y.; Ke, R.-J.; Jiang, P.-R.; Ying, J.-H.; Lou, E.-Z.; Chen, J.-Y. The effects of tectochrysin on prostate cancer cells apoptosis and its mechanism. *Chin. J. Appl. Physiol.* **2019**, *35*, 283.
363. Oh, S.-B.; Hwang, C.J.; Song, S.-Y.; Jung, Y.Y.; Yun, H.-M.; Sok, C.H.; Sung, H.C.; Yi, J.-M.; Park, D.H.; Ham, Y.W. Anti-cancer effect of tectochrysin in NSCLC cells through overexpression of death receptor and inactivation of STAT3. *Cancer Lett.* **2014**, *353*, 95–103. [CrossRef]
364. Zhang, H.; Xie, B.; Zhang, Z.; Sheng, X.; Zhang, S. Tetrandrine suppresses cervical cancer growth by inducing apoptosis In Vitro and In Vivo. *Drug Des. Devel. Ther.* **2019**, *13*, 119. [CrossRef]
365. Wang, C.H.; Yang, J.M.; Guo, Y.B.; Shen, J.; Pei, X.H. Anticancer activity of tetrandrine by inducing apoptosis in human breast cancer cell line MDA-MB-231 In Vivo. *Evid. Based Complement. Alternat. Med.* **2020**, *2020*, 6823520. [CrossRef]
366. Qin, R.; Shen, H.; Cao, Y.; Fang, Y.; Li, H.; Chen, Q.; Xu, W. Tetrandrine induces mitochondria-mediated apoptosis in human gastric cancer BGC-823 cells. *PLoS ONE* **2013**, *8*, e76486. [CrossRef]
367. Tsai, S.-C.; Wu, W.-C.; Yang, J.-S. Tetrandrine Inhibits Epithelial-Mesenchymal Transition in IL-6-Induced HCT116 Human Colorectal Cancer Cells. *Onco Targets Ther.* **2021**, *14*, 4523. [CrossRef]
368. Shishodia, G.; Koul, S.; Dong, Q.; Koul, H.K. Tetrandrine (TET) induces death receptors Apo Trail R1 (DR4) and Apo Trail R2 (DR5) and sensitizes prostate cancer cells to TRAIL-induced apoptosis. *Mol. Cancer Ther.* **2018**, *17*, 1217–1228. [CrossRef]
369. Wang, N.; Yang, S.; Tan, T.; Huang, Y.; Chen, Y.; Dong, C.; Chen, J.; Luo, X. Tetrandrine suppresses the growth of human osteosarcoma cells by regulating multiple signaling pathways. *Bioengineered* **2021**, *12*, 5870–5882. [CrossRef]
370. Elbe, H.; Yigitturk, G.; Cavusoglu, T.; Uyanikgil, Y.; Ozturk, F. Apoptotic effects of thymol, a novel monoterpene phenol, on different types of cancer. *Bratisl. Lek. Listy* **2020**, *121*, 122–128. [CrossRef]

371. Zeng, Q.; Che, Y.; Zhang, Y.; Chen, M.; Guo, Q.; Zhang, W. Thymol Isolated from Thymus vulgaris L. inhibits colorectal cancer cell growth and metastasis by suppressing the Wnt/β-catenin pathway. *Drug Des. Devel. Ther.* **2020**, *14*, 2535. [CrossRef]
372. Kang, S.-H.; Kim, Y.-S.; Kim, E.-K.; Hwang, J.-W.; Jeong, J.-H.; Dong, X.; Lee, J.-W.; Moon, S.-H.; Jeon, B.-T.; Park, P.-J. Anticancer effect of thymol on AGS human gastric carcinoma cells. *J. Microbiol. Biotechnol.* **2016**, *26*, 28–37. [CrossRef]
373. Dera, A.; Rajagopalan, P. Thymoquinone attenuates phosphorylation of AKT to inhibit kidney cancer cell proliferation. *J. Food Biochem.* **2019**, *43*, e12793. [CrossRef]
374. Woo, C.C.; Hsu, A.; Kumar, A.P.; Sethi, G.; Tan, K.H.B. Thymoquinone inhibits tumor growth and induces apoptosis in a breast cancer xenograft mouse model: The role of p38 MAPK and ROS. *PLoS ONE* **2013**, *8*, e75356. [CrossRef]
375. Iskender, B.; Izgi, K.; Hizar, E.; Jauch, J.; Arslanhan, A.; Yuksek, E.H.; Canatan, H. Inhibition of epithelial-mesenchymal transition in bladder cancer cells via modulation of mTOR signalling. *Tumor Biol.* **2016**, *37*, 8281–8291. [CrossRef]
376. Kundu, J.; Choi, B.Y.; Jeong, C.-H.; Kundu, J.K.; Chun, K.-S. Thymoquinone induces apoptosis in human colon cancer HCT116 cells through inactivation of STAT3 by blocking JAK2-and Src-mediated phosphorylation of EGF receptor tyrosine kinase. *Oncol. Rep.* **2014**, *32*, 821–828. [CrossRef]
377. Zhu, W.-Q.; Wang, J.; Guo, X.-F.; Liu, Z.; Dong, W.-G. Thymoquinone inhibits proliferation in gastric cancer via the STAT3 pathway In Vivo and In Vitro. *World J. Gastroenterol.* **2016**, *22*, 4149. [CrossRef]
378. Ashour, A.E.; Abd-Allah, A.R.; Korashy, H.M.; Attia, S.M.; Alzahrani, A.Z.; Saquib, Q.; Bakheet, S.A.; Abdel-Hamied, H.E.; Jamal, S.; Rishi, A.K. Thymoquinone suppression of the human hepatocellular carcinoma cell growth involves inhibition of IL-8 expression, elevated levels of TRAIL receptors, oxidative stress and apoptosis. *Mol. Cell. Biochem.* **2014**, *389*, 85–98. [CrossRef]
379. Yang, J.; Kuang, X.R.; Lv, P.T.; Yan, X.X. Thymoquinone inhibits proliferation and invasion of human nonsmall-cell lung cancer cells via ERK pathway. *Tumor Biol.* **2015**, *36*, 259–269. [CrossRef]
380. Abdelfadil, E.; Cheng, Y.-H.; Bau, D.-T.; Ting, W.-J.; Chen, L.-M.; Hsu, H.-H.; Lin, Y.-M.; Chen, R.-J.; Tsai, F.-J.; Tsai, C.-H. Thymoquinone induces apoptosis in oral cancer cells through p38β inhibition. *Am. J. Chin. Med.* **2013**, *41*, 683–696. [CrossRef]
381. Torres, M.P.; Ponnusamy, M.P.; Chakraborty, S.; Smith, L.M.; Das, S.; Arafat, H.A.; Batra, S.K. Effects of thymoquinone in the expression of mucin 4 in pancreatic cancer cells: Implications for the development of novel cancer therapies. *Mol. Cancer Ther.* **2010**, *9*, 1419–1431. [CrossRef]
382. Lin, W.; Ye, H. Anticancer activity of ursolic acid on human ovarian cancer cells via ROS and MMP mediated apoptosis, cell cycle arrest and downregulation of PI3K/AKT pathway. *J. BUON* **2020**, *25*, 750–756.
383. Chen, C.-J.; Shih, Y.-L.; Yeh, M.-Y.; Liao, N.-C.; Chung, H.-Y.; Liu, K.-L.; Lee, M.-H.; Chou, P.-Y.; Hou, H.-Y.; Chou, J.-S. Ursolic acid induces apoptotic cell death through AIF and endo G release through a mitochondria-dependent pathway in NCI-H292 human lung cancer cells In Vitro. *In Vivo* **2019**, *33*, 383–391. [CrossRef] [PubMed]
384. Wang, W.; Zhao, C.; Jou, D.; Lü, J.; Zhang, C.; Lin, L.; Lin, J. Ursolic acid inhibits the growth of colon cancer-initiating cells by targeting STAT3. *Anticancer Res.* **2013**, *33*, 4279–4284. [PubMed]
385. Zhang, X.; Li, T.; Gong, E.S.; Liu, R.H. Antiproliferative activity of ursolic acid in MDA-MB-231 human breast cancer cells through Nrf2 pathway regulation. *J. Agric. Food Chem.* **2020**, *68*, 7404–7415. [CrossRef] [PubMed]
386. Prasad, S.; Yadav, V.R.; Sung, B.; Gupta, S.C.; Tyagi, A.K.; Aggarwal, B.B. Ursolic acid inhibits the growth of human pancreatic cancer and enhances the antitumor potential of gemcitabine in an orthotopic mouse model through suppression of the inflammatory microenvironment. *Oncotarget* **2016**, *7*, 13182. [CrossRef]
387. Weng, H.; Tan, Z.-J.; Hu, Y.-P.; Shu, Y.-J.; Bao, R.-F.; Jiang, L.; Wu, X.-S.; Li, M.-L.; Ding, Q.; Wang, X.-a. Ursolic acid induces cell cycle arrest and apoptosis of gallbladder carcinoma cells. *Cancer Cell Int.* **2014**, *14*, 1–10. [CrossRef]
388. Zúñiga, R.; Concha, G.; Cayo, A.; Cikutović-Molina, R.; Arevalo, B.; González, W.; Catalán, M.A.; Zúñiga, L. Withaferin A suppresses breast cancer cell proliferation by inhibition of the two-pore domain potassium (K2P9) channel TASK-3. *Biomed. Pharmacother.* **2020**, *129*, 110383. [CrossRef]
389. Yang, I.-H.; Kim, L.-H.; Shin, J.-A.; Cho, S.-D. Chemotherapeutic effect of withaferin A in human oral cancer cells. *J. Cancer Ther.* **2015**, *6*, 735. [CrossRef]
390. Nagy, Z.; Cheung, B.B.; Tsang, W.; Tan, O.; Herath, M.; Ciampa, O.C.; Shadma, F.; Carter, D.R.; Marshall, G.M. Withaferin A activates TRIM16 for its anti-cancer activity in melanoma. *Sci. Rep.* **2020**, *10*, 1–9. [CrossRef]
391. Chen, Y.; Han, X.Z.; Wang, W.; Zhao, R.T.; Li, X. Withaferin A inhibits osteosarcoma cells through inactivation of Notch-1 signaling. *Bangladesh J. Pharmacol.* **2014**, *9*, 364–370. [CrossRef]
392. Choi, B.Y.; Kim, B.-W. Withaferin-A inhibits colon cancer cell growth by blocking STAT3 transcriptional activity. *J. Cancer Prev.* **2015**, *20*, 185. [CrossRef]
393. Feng, Q.; Wang, H.; Pang, J.; Ji, L.; Han, J.; Wang, Y.; Qi, X.; Liu, Z.; Lu, L. Prevention of wogonin on colorectal cancer tumorigenesis by regulating p53 nuclear translocation. *Front. Pharmacol.* **2018**, *9*, 1356. [CrossRef]
394. Yang, L.; Zhang, H.W.; Hu, R.; Yang, Y.; Qi, Q.; Lu, N.; Liu, W.; Chu, Y.Y.; You, Q.D.; Guo, Q.L. Wogonin induces G1 phase arrest through inhibiting Cdk4 and cyclin D1 concomitant with an elevation in p21Cip1 in human cervical carcinoma HeLa cells. *Biochem. Cell Biol.* **2009**, *87*, 933–942. [CrossRef]
395. Shi, G.; Wang, Q.; Zhou, X.; Li, J.; Liu, H.; Gu, J.; Wang, H.; Wu, Y.; Ding, L.; Ni, S. Response of human non-small-cell lung cancer cells to the influence of Wogonin with SGK1 dynamics. *Acta Biochim. Biophys. Sin.* **2017**, *49*, 302–310. [CrossRef]
396. Koh, H.; Sun, H.-N.; Xing, Z.; Liu, R.; Chandimali, N.; Kwon, T.; Lee, D.-S. Wogonin Influences Osteosarcoma Stem Cell Stemness Through ROS-dependent Signaling. *Vivo* **2020**, *34*, 1077–1084. [CrossRef]

397. Yu, J.S.; Kim, A.K. Wogonin induces apoptosis by activation of ERK and p38 MAPKs signaling pathways and generation of reactive oxygen species in human breast cancer cells. *Mol. Cells* **2011**, *31*, 327–335. [CrossRef]
398. Ruibin, J.; Bo, J.; Danying, W.; Chihong, Z.; Jianguo, F.; Linhui, G. Therapy effects of wogonin on ovarian cancer cells. *BioMed Res. Int.* **2017**, *2017*, 9381513. [CrossRef]
399. Li, W.D.; Wu, Y.; Zhang, L.; Yan, L.G.; Yin, F.Z.; Ruan, J.S.; Chen, Z.P.; Yang, G.M.; Yan, C.P.; Zhao, D. Characterization of xanthatin: Anticancer properties and mechanisms of inhibited murine melanoma In Vitro and In Vivo. *Phytomedicine* **2013**, *20*, 865–873. [CrossRef]
400. Tao, L.; Sheng, X.; Zhang, L.; Li, W.; Wei, Z.; Zhu, P.; Zhang, F.; Wang, A.; Woodgett, J.R.; Lu, Y. Xanthatin anti-tumor cytotoxicity is mediated via glycogen synthase kinase-3β and β-catenin. *Biochem. Pharmacol.* **2016**, *115*, 18–27. [CrossRef]
401. Yu, Y.; Yu, J.; Pei, C.G.; Li, Y.Y.; Tu, P.; Gao, G.P.; Shao, Y. Xanthatin, a novel potent inhibitor of VEGFR2 signaling, inhibits angiogenesis and tumor growth in breast cancer cells. *Int. J. Clin. Exp. Pathol.* **2015**, *8*, 10355.
402. Li, L.; Liu, P.; Xie, Y.; Liu, Y.; Chen, Z.; Geng, Y.; Zhang, L. Xanthatin inhibits human colon cancer cells progression via mTOR signaling mediated energy metabolism alteration. *Drug Dev. Res.* **2021**, *83*, 119–130. [CrossRef]
403. Newman, D.J.; Cragg, G.M. Natural products as sources of new drugs from 1981 to 2014. *J. Nat. Prod.* **2016**, *79*, 629–661. [CrossRef]
404. Vallianou, N.G.; Evangelopoulos, A.; Schizas, N.; Kazazis, C. Potential anticancer properties and mechanisms of action of curcumin. *Anticancer Res.* **2015**, *35*, 645–651.
405. Zheng, B.; McClements, D.J. Formulation of more efficacious curcumin delivery systems using colloid science: Enhanced solubility, stability, and bioavailability. *Molecules* **2020**, *25*, 2791. [CrossRef]
406. Venkatesan, P.; Rao, M. Structure-activity relationships for the inhibition of lipid peroxidation and the scavenging of free radicals by synthetic symmetrical curcumin analogues. *J. Pharm. Pharmacol.* **2000**, *52*, 1123–1128. [CrossRef]
407. Youssef, K.M.; El-Sherbeny, M.A.; El-Shafie, F.S.; Farag, H.A.; Al-Deeb, O.A.; Awadalla, S.A.A. Synthesis of curcumin analogues as potential antioxidant, cancer chemopreventive agents. *Arch. Pharm.* **2004**, *337*, 42–54. [CrossRef]
408. Ohtsu, H.; Itokawa, H.; Xiao, Z.; Su, C.-Y.; Shih, C.C.-Y.; Chiang, T.; Chang, E.; Lee, Y.; Chiu, S.-Y.; Chang, C. Antitumor agents 222. Synthesis and anti-androgen activity of new diarylheptanoids. *Biorg. Med. Chem.* **2003**, *11*, 5083–5090. [CrossRef]
409. Ohtsu, H.; Xiao, Z.; Ishida, J.; Nagai, M.; Wang, H.-K.; Itokawa, H.; Su, C.-Y.; Shih, C.; Chiang, T.; Chang, E. Antitumor agents. 217. Curcumin analogues as novel androgen receptor antagonists with potential as anti-prostate cancer agents. *J. Med. Chem.* **2002**, *45*, 5037–5042. [CrossRef]
410. Itokawa, H.; Shi, Q.; Akiyama, T.; Morris-Natschke, S.L.; Lee, K.H. Recent advances in the investigation of curcuminoids. *Chin. Med.* **2008**, *3*, 1–13. [CrossRef]
411. Lin, L.; Lee, K.-H. Structure-activity relationships of curcumin and its analogs with different biological activities. *Stud. Nat. Prod. Chem.* **2006**, *33*, 785–812.
412. Morris, J.; Moseley, V.R.; Cabang, A.B.; Coleman, K.; Wei, W.; Garrett-Mayer, E.; Wargovich, M.J. Reduction in promotor methylation utilizing EGCG (epigallocatechin-3-gallate) restores RXRα expression in human colon cancer cells. *Oncotarget* **2016**, *7*, 35313. [CrossRef]
413. Lambert, J.D.; Elias, R.J. The antioxidant and pro-oxidant activities of green tea polyphenols: A role in cancer prevention. *Arch. Biochem. Biophys.* **2010**, *501*, 65–72. [CrossRef] [PubMed]
414. Min, K.-j.; Kwon, T.K. Anticancer effects and molecular mechanisms of epigallocatechin-3-gallate. *Integr. Med. Res.* **2014**, *3*, 16–24. [CrossRef] [PubMed]
415. Landis-Piwowar, K.R.; Kuhn, D.J.; Wan, S.B.; Chen, D.; Chan, T.H.; Dou, Q.P. Evaluation of proteasome-inhibitory and apoptosis-inducing potencies of novel (-)-EGCG analogs and their prodrugs. *Int. J. Mol. Med.* **2005**, *15*, 735–742. [CrossRef]
416. Khandelwal, A.; Hall, J.A.; Blagg, B.S. Synthesis and structure–activity relationships of EGCG analogues, a recently identified Hsp90 inhibitor. *J. Org. Chem.* **2013**, *78*, 7859–7884. [CrossRef] [PubMed]
417. Matsubara, S.; Shibata, H.; Ishikawa, F.; Yokokura, T.; Takahashi, M.; Sugimura, T.; Wakabayashi, K. Suppression of Helicobacter pylori-induced gastritis by green tea extract in Mongolian gerbils. *Biochem. Biophys. Res. Commun.* **2003**, *310*, 715–719. [CrossRef] [PubMed]
418. Iqbal, J.; Abbasi, B.A.; Mahmood, T.; Kanwal, S.; Ali, B.; Shah, S.A.; Khalil, A.T. Plant-derived anticancer agents: A green anticancer approach. *Asian Pac. J. Trop. Biomed.* **2017**, *7*, 1129–1150. [CrossRef]
419. Yang, Z.; Kulkarni, K.; Zhu, W.; Hu, M. Bioavailability and pharmacokinetics of genistein: Mechanistic studies on its. *Anticancer Agents Med. Chem.* **2012**, *12*, 1264–1280. [CrossRef]
420. Papaj, K.; Kasprzycka, A.; Góra, A.; Grajoszek, A.; Rzepecka, G.; Stojko, J.; Barski, J.-J.; Szeja, W.; Rusin, A. Structure–bioavailability relationship study of genistein derivatives with antiproliferative activity on human cancer cell. *J. Pharm. Biomed. Anal.* **2020**, *185*, 113216. [CrossRef]
421. Byczek, A.; Zawisza-Puchalka, J.; Gruca, A.; Papaj, K.; Grynkiewicz, G.; Rusin, M.; Szeja, W.; Rusin, A. Genistein derivatives regioisomerically substituted at 7-O-and 4′-O-have different effect on the cell cycle. *J. Chem.* **2013**, *2013*, 191563. [CrossRef]
422. Szeja, W.; Grynkiewicz, G.; Bieg, T.; Swierk, P.; Byczek, A.; Papaj, K.; Kitel, R.; Rusin, A. Synthesis and cytotoxicity of 2, 3-enopyranosyl C-linked conjugates of genistein. *Molecules* **2014**, *19*, 7072–7093. [CrossRef]
423. Nahum, A.; Hirsch, K.; Danilenko, M.; Watts, C.K.; Prall, O.W.; Levy, J.; Sharoni, Y. Lycopene inhibition of cell cycle progression in breast and endometrial cancer cells is associated with reduction in cyclin D levels and retention of p27 Kip1 in the cyclin E–cdk2 complexes. *Oncogene* **2001**, *20*, 3428–3436. [CrossRef]

424. Carini, F.; David, S.; Tomasello, G.; Mazzola, M.; Damiani, P.; Rappa, F.; Battaglia, L.; Cappello, F.; Jurjus, A.; Geagea, A.G. Colorectal cancer: An update on the effects of lycopene on tumor progression and cell proliferation. *J. Biol. Regul. Homeost. Agents* **2017**, *31*, 769–774. [PubMed]
425. Ben-Dor, A.; Steiner, M.; Gheber, L.; Danilenko, M.; Dubi, N.; Linnewiel, K.; Zick, A.; Sharoni, Y.; Levy, J. Carotenoids activate the antioxidant response element transcription system. *Mol. Cancer Ther.* **2005**, *4*, 177–186.
426. Linnewiel, K.; Ernst, H.; Caris-Veyrat, C.; Ben-Dor, A.; Kampf, A.; Salman, H.; Danilenko, M.; Levy, J.; Sharoni, Y. Structure activity relationship of carotenoid derivatives in activation of the electrophile/antioxidant response element transcription system. *Free Radic. Biol. Med.* **2009**, *47*, 659–667. [CrossRef]
427. Yang, Y.; Zhang, G.; Li, C.; Wang, S.; Zhu, M.; Wang, J.; Yue, H.; Ma, X.; Zhen, Y.; Shu, X. Metabolic profile and structure–activity relationship of resveratrol and its analogs in human bladder cancer cells. *Cancer Manag. Res.* **2019**, *11*, 4631. [CrossRef]
428. Herath, W.; Khan, S.I.; Khan, I.A. Microbial metabolism. Part 14. Isolation and bioactivity evaluation of microbial metabolites of resveratrol. *Nat. Prod. Res.* **2013**, *27*, 1437–1444. [CrossRef]