Chinese Herbal Medicines 14 (2022) 210–233

Contents lists available at ScienceDirect

Chinese Herbal Medicines

journal homepage: www.elsevier.com/locate/chmed

Review

# Genus *Tetrastigma*: A review of its folk uses, phytochemistry and pharmacology

Lizhi Zhang [a,1], Bin Li [a,1], Mengyun Wang [a], Haotian Lin [a], Yilin Peng [a], Xudong Zhou [a], Caiyun Peng [a], Jixun Zhan [b,*], Wei Wang [a,*]

[a] *TCM and Ethnomedicine Innovation & Development International Laboratory, Academician Atta-ur-Rahman Belt and Road Traditional Medicine Research Center, School of Pharmacy, Hunan University of Chinese Medicine, Changsha 410208, China*
[b] *Department of Biological Engineering, Utah State University, Logan, UT 84322-4105, United States*

A R T I C L E   I N F O

*Article history:*
Received 15 November 2021
Revised 27 December 2021
Accepted 17 January 2022
Available online 17 March 2022

*Keywords:*
chemical constituents
clinical applications
folk uses
pharmacological activity
*Tetrastigma genus*

A B S T R A C T

The genus *Tetrastigma* belongs to the Vitaceae family and contains over 100 species. This paper reviewed folk uses, chemical constituents, pharmacological activities, and clinical applications of the medicinal plants in the genus *Tetrastigma*. In addition, the paper also discussed the current problems for the further studies. Up to now, more than 240 compounds were reported from the genus *Tetrastigma*, covering 74 flavonoids, 14 terpenoids, 19 steroids, 21 phenylpropanoids, 14 alkaloids and others constituents. Among them, flavonoids are the major and the characteristic chemical constituents in this genus. Modern pharmacological studies and clinical practice showed that the extracts and chemical constituents of *Tetrastigma* species possessed wide pharmacological activities including antitumor, antioxidative, hepatoprotective, antiviral, anti-inflammatory, and analgesic activities. The information summarized in this paper provides valuable clues for new drug discovery and an incentive to expand the research of genus *Tetrastigma*.



**Contents**



* Corresponding authors.
*E-mail addresses:* jixun.zhan@usu.edu (J.x. Zhan), wangwei402@hotmail.com (W. Wang).
[1] These authors contributed equally to this work.

https://doi.org/10.1016/j.chmed.2022.03.003
1674-6384/

## 1. Introduction

*Tetrastigma* (Vitaceae) contains over 100 species widely spreading in Asia and Oceania. Among them, 45 species are distributed in China, mainly in Guangdong, Yunnan and Zhejiang Provinces and Guangxi autonomous region, in China (Zhang et al., 2019). Some *Tetrastigma* species have a long history as ethnomedicines for the treatment of many diseases, such as menstrual disorders, rheumatic pain, bruises, gastralgia and other diseases in southwest China. These medicinal plants with remarkable curative effects were deeply loved by local people, especially *Tetrastigma hemsleyanum* Diels et Gilg, which was awarded as one of the new ''eight famous TCMs'' in Zhejiang Province (Ji et al., 2021). The medicinal plants in this genus attracted increasing attention due to their structural diversity and remarkable pharmacological activities. Besides, many studies showed that the crude extracts and the monomeric compounds from *Tetrastigma* species exhibited diverse biological activities, such as antitumor, antioxidative, hepatoprotective, antiviral, anti-inflammatory, and analgesic activities (Fig. 1). The chemical and pharmacological research on this genus is limited, except the species *T. hemsleyanum*. In order to provide theoretical reference for further research and to comprehensively understand the medicinal applications on this genus, this paper systematically reviewed folk uses, chemical constituents, pharmacological activities and clinical applications of *Tetrastigma* species based on available databases including SciFinder, Pubmed, Google Scholar, CNKI and others over the past 20 years.

## 2. Folk uses

In China, many *Tetrastigma* species are traditionally and ethnically used as folk medicine to treat various diseases for a long time. Some species have a long medicinal history, such as *T. hemsleyanum*, known as ''Sanyeqing'' or ''Jingxiandiaohulu'' (Cheng & Fu, 2016), *T. hypoglaucum* Planch, known as ''Wuzhuajinlong'' (Liu, 2000), and *T. obtectum* (Wall.) Planch, known as ''Yanwujia'' (Shi, 2012) in Chinese. *T. hemsleyanum* was firstly recorded in *Ben Cao Gang Mu* (*Compendium of Materia Medica*) (Ming Dynasty, CE 1590) and also recorded in multiple ancient books of traditional Chinese medicine (TCM), including *Zhi Wu Ming Shi Tu Kao* (*Chih-wu ming-shih t'u kao*) (Qing Dynasty, Wu, 2014), *Jiangxi Herbal Medicine* and *Common Folk Herbal Medicine* in Zhejiang (Ji et al., 2021). These ancient works described that its root tuber or whole plant could be used as medicine and it was slightly bitter in flavor and neutral in nature. It had the effect of strengthening liver, and its functions were mainly for clearing heat and detoxification, dispelling wind and phlegm, promoting blood circulation and relieving pain. *T. hypoglaucum* was recorded in The *Dictionary of Chinese Herbal Medicine*. Its root or whole plant could be used as medicine and it was bitter, neutral in nature. *Tetrastigma planicaule* (Hook.) Gagnep was recorded in *Handbook of Chinese Herbal Medicine in Guangzhou Army*. It was one of 108 classic medicines in Yao ethnomedicine (Shao, 2011). The whole plant was used as medicine and it was pungent, astringent in flavor and warm in nature. Its main function was to dispel wind and dehumidify, relax ten-

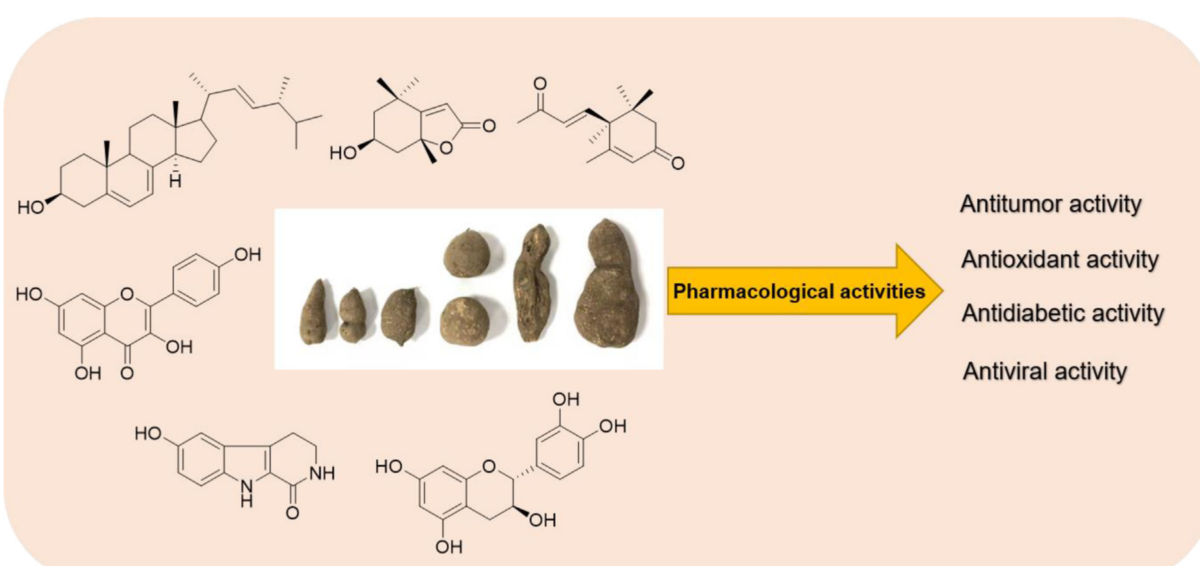


**Fig. 1.** Chemical components, pharmacological activities of medicinal parts from *Tetrastigma*.

**Table 1**
Sources, distribution and folk uses of *Tetrastigma* medicinal plants.

| Species | Folk names | Distribution | Medicinal parts | Folk uses |
|---|---|---|---|---|
| *Tetrastigma hemsleyanum* Diels et Gilg | Sanyeqing (Cai et al., 2014) (Chinese) | The areas south of Yangtze River, mainly distributed in Zhejiang, Jiangxi, Jiangsu, Fujian, Hunan, Hubei, Guangdong, Guangxi, Yunnan of China and other areas (Qian et al., 2015). | Root tuber or whole plant | Children with febrile convulsion, viral meningitis, asthma, pneumonia, nephritis, hepatitis, rheumatism arthralgia, menstrual disorders and other diseases; external use for poisonous snake bite, amygdalitis, ulcerative carbuncle, phlegmon, traumatic injury and so on (Wang et al., 2015); Yao ethnomedicine: urinary tract stones, gallstones, renal calculi, gastralgia and other diseases. |
| *Tetrastigrna hypoglaucum* Planch | Wuzhuajinlong (Liu, 2000) (Chinese) | Sichuan, Yunnan and other provinces (Liu, 2000) of China. | Root or whole plant | Fracture and tendon injury, traumatic injury, rheumatic swelling and pain and other diseases (Liu, 2000). |
| *Tetrastigma obtectum* (Wall.) Planch | Zouyoucao (Song and Wan, 2003). (Chinese) | Yunnan, Gansu, Hunan, Fujian, Taiwan, Guangxi, Sichuan, Guizhou Provinces of China (Shi, 2012). | | Tujia ethnomedicine: rheumatic pain, traumatic injury, osteomyelitis, menstrual disorders, lumbar muscle strain, snake bite and other diseases (Shi, 2012). |
| *Tetrastigma planicaule* (Hook.) Gagnep | Biandanteng (Chen, 2017). (Chinese) | Fujian, Guangdong, Guangxi, Guizhou, Yunnan, southeastern Tibet of China (Shao et al., 2010). | Whole plant | Zhuang ethnomedicine, Yao ethnomedicine and other nationalities; common use for rheumatic bone pain, lumbar muscle strain, traumatic injury, hemiplegia (Shao, 2011). |
| *Tetrastigma erubescens* Planch | – | Viet nam, Kampuchea and Guangxi, Hainan, Yunnan, Guangdong and other areas in China. | – | Inflammation, fever, gastralgia, hypertension and other diseases (Dao et al. 2014). |

dons and activate collaterals. *T. obtectum* was recorded in *Si Chuan Zhong Yao Zhi* (a dictionary of Chinese medicine). Its root or whole plant could be used as medicine and it was warm in nature, pungent in taste, and non-toxic. The functions were mainly for dispelling wind, dehumidification and detoxification. Out of the 100 species of *Tetrastigma* identified, only five species were reported in folk medicines as medicinal plants. Moreover, *T. hemsleyanum* was the one that was most widely used and studied. The folk names, geographical distribution, medicinal parts and folk uses of the genus *Tetrastigma* are listed in Table 1.

## 3. Chemical constituents

So far, a total of 248 compounds were isolated from five *Tetrastigma* species (*T. hemsleyanum*, *T. hypoglaucum*, *T.obtectum*, *T. planicaule*, and *T. erubescens*), including flavonoids and their glycosides (**1**–**74**), saccharides **(75**–**91**), terpenoids (**92**–**105**), steroids (**106**–**124**), phenylpropanoids (**125**–**145**), alkaloids (**146**–**159**) and other compounds. Flavonoids and their glycosides are the major constituents in the genus *Tetrastigma* and also exhibit significant antitumor activity, which are the research hotspots now. The information about chemical names, sources, and references of all compounds is summarized in Table 2.

### *3.1. Flavonoids*

Flavonoids are major and characteristic chemical components of the genus *Tetrastigma*. Thus far, more than 70 flavonoids were isolated in this genus and most of them are flavonoid carbon glycoside compounds. According to the conformation, they could be divided into four types: flavones (**1**–**38**), flavonols (**39**–**62**), flavanones (**69**), and flavan-3-ols (**65**–**66** and **70**–**74**). The aglycones of these flavonoids are mainly kaempferol (**45**), apigenin (**1**), orientin (**26**), vitexin (**28**), isorhamnetin (**42**) and quercetin (**55**). Most sugar moieties of flavonoid glycosides are glucose, rhamnose and xylose, which are typically connected to C-3, C-6, C-7 or C-8. What's more, there are oxygen-containing substituents at the C-7, such as OH, OMe or glycosyl in most of the flavonoid carbon glycosides. The names and sources of these compounds are shown in Table 2, and the structures are shown in Fig. 2.

#### *3.1.1. Flavones*

Up to now, 38 flavones and their glycosides (**1**–**38**) were reported from the genus *Tetrastigma.* The features of these compounds are that there are usually hydroxyl groups at the C-5 and C-7, and their aglycones mainly are apigenin (**1**), orientin (**26**), vitexin (**28**), and isorhamnetin (**42**). Furthermore, this series of compounds are mainly flavone carbon glycosides with glycosyl moieties connected at C-6 or C-8. Apigenin-6-*C*-α-*L*-rhmnnopyranosyl-(1-4)-α-*L*-arabinopymnoside (**2**) and apigenin-8-*C*-α-*L*-rhmnnopyranosyl-(1-4)-α-*L*-arabinopymnoside (**3**) were new natural products from *T. hemsleyanum*. Five new flavones (**6**–**8** and **37**–**38**) were isolated from stems and leaves of *T. obtectum*.

#### *3.1.2. Flavonols*

The phytochemical studies led to isolation and identification of 24 flavonols and their glycosides (**39**–**62**) from this genus. These series of compounds were mainly found in *T. hemsleyanum*, and they are mono-*O*-glycosides and di-*O*-glycosides, and the glycosyls are connected to C-3 or C-7. And their aglycones mainly were kaempferol (**45**) and quercetin (**55**). There are oxygen-containing substituents at the C-3' and C-4' of these flavonoid oxygen glycosides, such as OH and OMe.

#### *3.1.3. Flavanones, dihydrochalcone and flavan-3-ols*

Apart from flavonoids and flavonols, there are ten compounds of other types, including one dihydrochalcone (**68**), two flavanone (**63** and **69**), and eight flavan-3-ols (**65**–**67** and **70**–**74**). Compounds **71**–**74** isolated from *T. hemsleyanum* are flavan-3-ol derivatives tannins.

### *3.2. Polysaccharides and monosaccharides*

Polysaccharides and monosaccharides are also important constituents in *Tetrastigma* species. Previous studies indicated that polysaccharides had hypoglycemic and immunoregulatory activity.

**Table 2**
Names and sources of compounds isolated from genus *Tetrastigma*.

| No. | Chemical names | Source plants | Distribution in plant | References |
|---|---|---|---|---|
| **Flavonoids** | | | | |
| **1** | Apigenin | *T. hemsleyanum* | Whole plant | Lin et al. (2015) |
| **2** | Apigenin-6-*C*-α-*L*-rhmnnopyranosyl-(1-4)-α-*L*-arabinopymnoside | *T. hemsleyanum* | Aerial part | Liu et al. (2002) |
| **3** | Apigenin-8-*C*-α-*L*-rhamnopyranosyl-(1-4)-α-*L*-arabinopymnoside | *T. hemsleyanum* | Aerial part | Liu et al. (2002) |
| **4** | Apigenin-6,8-di-*C*-β-*D*-glucopyranoside | *T. hemsleyanum* | Aerial part | Liu (2000) |
| **5** | Apigenin-8-*C*-α-*L*-rhamnopyranosyl-(1-2)-β-*D*-glucopyranoside | *T. hemsleyanum* | Whole plants | Lin et al. (2015) |
| **6** | Apigenin-8-*C*-[6-deoxy-2-*O*-(α-*L*-rhamnopyranosyl)-*xylo*-hexopyranos-3-uloside] | *T. obtectum* | Stem and leaf | Shi (2012) |
| **7** | Apigenin-8-*C*-[α-*L*-rhamnopyranosyl(1 → 2)]-rhamnopyranoside] | *T. obtectum* | Stem and leaf | Shi (2012) |
| **8** | Apigenin-8-*C*-[α-*L*-rhamnopyranosyl(1 → 2)-xyloside] | *T. obtectum* | Stem and leaf | Shi (2012) |
| **9** | Apigenin-7-*O*-β-*D*-glucopyranoside | *T. obtectum* | Stem and leaf | Shi (2012) |
| **10** | Apigenin-6-*C*-α-*L*-arabinopyranoside | *T. obtectum* | Stem and leaf | Shi (2012) |
| **11** | Apigenin-6-*C*-α-*L*-arabinose-8-*C*-β-*D*-glucose | *T. hemsleyanum* | Aerial part | Sun (2018a) |
| **12** | Apigenin-7-rhamnoside | *T. hemsleyanum* | Root tuber and leaf | Sun (2018a) |
| **13** | Apigenin-8-*C*-xylosyl-6-*C*-glucoside | *T. hemsleyanum* | Aerial part | Sun (2018a) |
| **14** | Biochanin A | *T. hemsleyanum* | Root tuber | Sun (2018a) |
| **15** | Daidzein | *T. hemsleyanum* | Root tuber | Sun (2018a) |
| **16** | Isoorientin | *T. hemsleyanum* | Aerial part | Sun (2018a) |
| **17** | Isoorientin-2″-*O*-rhamnoside | *T. hemsleyanum* | Aerial part | Sun (2018a) |
| **18** | Isoorientin-4″-*O*-xyloside | *T. hemsleyanum* | Aerial part | Sun (2018a) |
| **19** | Isovitexin | *T. hemsleyanum* | Aerial part | Sun (2018a) |
| **20** | Isovitexin-2″-*O*-rhamnoside | *T. hemsleyanum* | Aerial part | Sun (2018a) |
| **21** | Isovitexin-2″-*O*-xyloside | *T. hemsleyanum* | Aerial part | Sun (2018a) |
| **22** | Isoamylbenzoicacid-4-*O*-xylosyl glucoside | *T. hemsleyanum* | Root tuber | Wang et al. (2018) |
| **23** | Luteolin | *T. hemsleyanum* | Aerial part | Sun (2018a) |
| **24** | Luteolin-6,8-di-*C*-hexoside | *T. hemsleyanum* | Aerial part | Sun (2018a) |
| **25** | Luteolin-7-*O*-β-*D*-glucopyranoside | *T. obtectum* | Stem and leaf | Shi (2012) |
| **26** | Orientin | *T. hemsleyanum* | Aerial part | Sun (2018a) |
| **27** | Orientin-2″-*O*-rhamnoside | *T. hemsleyanum* | Aerial part | Sun (2018a) |
| **28** | Vitexin | *T. hemsleyanum* | Aerial part | Sun et al. (2018) |
| **29** | Vitexin-2″-*O*-rhamnoside | *T. hemsleyanum* *T. obtectum* | Aerial part | Sun (2018a) |
| **30** | Vitexin-2″-*O*-arabinoside | *T. hemsleyanum* | Aerial part | Sun (2018a) |
| **31** | Vitexin-2″-*O*-glucoside | *T. hemsleyanum* | Aerial part | Sun (2018a) |
| **32** | Vitexin-α-*L*-rhamnoside | *T. obtectum* | Stem and leaf | Shi (2012) |
| **33** | Nobiletin | *T. erubescens* | Stem | Dao et al. (2014) |
| **34** | Tangeretin | *T. erubescens* | Stem | Dao et al. (2014) |
| **35** | 6-Demethoxytangeretin | *T. erubescens* | Stem | Dao et al. (2014) |
| **36** | 6-Demethoxynobiletin | *T. erubescens* | Stem | Dao et al. (2014) |
| **37** | *cis*-Apigenin-6-vinyl-7″-rhamnoside | *T. obtectum* | Stem and leaf | Shi (2012) |
| **38** | *cis*-Apigenin-8-vinyl-7″-rhamnoside | *T. obtectum* | Stem and leaf | Shi (2012) |
| **39** | Astragalin | *T. hemsleyanum* | Leaf | Sun (2018a) |
| **40** | Dingdingting-3-*O*-glucoside | *T. hemsleyanum* | Tuber | Zeng et al. (2017) |
| **41** | Isoquercitrin | *T. hemsleyanum* | Root tuber | Guo (2013) |
| **42** | Isorhamnetin | *T. hemsleyanum* | Root tuber | Zeng et al. (2017) |
| **43** | Isorhamnetin-3-rutinoside | *T. hemsleyanum* | Root tuber | Sun (2018a) |
| **44** | Isorhamnetin-7-*O*-rhamnose-3-*O*-glucoside | *T. hemsleyanum* | Root tuber | Zeng et al. (2017) |
| **45** | Kaempferol | *T. hemsleyanum* | Root tuber | Chen (2014) |
| **46** | Kaempferol-3-*O*-neohesperiodoside | *T. hemsleyanum* | Root tuber | Guo (2013) |
| **47** | Kaempferol-7-*O*-β-*L*-rhamnopyranosyl-3-*O*-β-*D*-glucopyranoside | *T. hemsleyanum* | Aerial part | Liu (2000) |
| **48** | Kaempferol-7-*O*-α-*L*-rhamnopyranoside | *T. hemsleyanum* | Leaf | Sun (2018a) |
| **49** | Kaempferide | *T. hemsleyanum* | Root tuber; aerial part | Sun (2018a) |
| **50** | Kaempferol-3-*O*-rutoside | *T. hemsleyanum* | Root tuber | Zeng et al. (2017) |
| **51** | Kaempferol-3-*O*-rhamnoside | *T. hemsleyanum* | Aerial part; root tuber | Sun et al. (2018) |
| **52** | Kaempferol-3-robinoside-7-rhamnoside | *T. hemsleyanum* | Root tuber | Sun (2018a) |
| **53** | Kaempferol-3-sambubioside | *T. hemsleyanum* | Root tuber; aerial part | Sun (2018a), Sun et al. (2018) |
| **54** | Kaempferitrin | *T. hemsleyanum* | Whole plant | Lin et al. (2015) |
| **55** | Quercetin | *T. hemsleyanum* | Root tuber | Chen (2014) |
| **56** | Quercitrin | *T. hemsleyanum* | Aerial part; root tuber | Sun et al. (2018), Zeng et al. (2017) |
| **57** | Quercetin-3-*O*-galactoside | *T. hemsleyanum* | Root tuber | Sun (2018a) |
| **58** | Quercetin-3-*O*-xylosylglucoside | *T. hemsleyanum* | Root tuber | Zeng et al. (2017) |
| **59** | Quercetin-3-*O*-xylosylglucoside-7-*O*-rhamnoside | *T. hemsleyanum* | Root tuber | Zeng et al. (2017) |
| **60** | Quercetin-3-*O*-rutinoside | *T. hemsleyanum* | Aerial part | Sun (2018a) |
| **61** | Rhamnocitrin | *T. hemsleyanum* | Root | Sun (2018a) |
| **62** | Rutin | *T. hemsleyanum* | Leaf | Sun (2018a) |
| **63** | Epicatechin-3-*O*-gallate | *T. erubescens* | Stem | Dao et al. (2014) |
| **64** | Catechin glucopyranoside isomer | *T. hemsleyanum* | Root | Sun (2018a) |
| **65** | (+)-Catechin | *T. erubescens*; *T. hemsleyanum*; *T. hypogtaucum* | Stem; aerial part | Dao et al. (2014), Zeng (2013), Liu (2000) |

(*continued on next page*)

**Table 2** (*continued*)

| No. | Chemical names | Source plants | Distribution in plant | References |
|---|---|---|---|---|
| **66** | Epigallocatechin | *T. hemsleyanum* | Tuber | Sun (2018a) |
| **67** | 7-Galloylcatechin | *T. hypoglaucum* | Aerial part | Liu (2000) |
| **68** | Phloridzin | *T. erubescens*; *T. hemsleyanum* | Stem; root tuber | Dao et al. (2014), Guo (2013) |
| **69** | Eriodictyol | *T. hemsleyanum* | Aerial part | Sun (2018a) |
| **70** | Aromadendrin | *T. hemsleyanum* | Root tuber | Guo (2013) |
| **71** | Procyanidin dimmer | *T. hemsleyanum* | Root tuber | Sun (2018a) |
| **72** | Procyanidin trimer | *T. hemsleyanum* | Aerial part | Sun et al. (2018), Zeng et al. (2017) |
| **73** | Procyanidins B1 | *T. hemsleyanum* | Aerial part; root tuber | Sun et al. (2018), Xu et al. (2014) |
| **74** | Procyanidins B2 | *T. hemsleyanum* | Aerial part; root tuber | Sun et al. (2018), Xu et al. (2014) |
| **Saccharides** | | | | |
| **75** | Arabinose | *T. hemsleyanum* | Root and leaf | Rao et al. (2016) |
| **76** | Fucose | *T. hemsleyanum* | Root and leaf | Rao et al. (2016) |
| **77** | Galactose | *T. hemsleyanum* | Root and Leaf | Rao et al. (2016) |
| **78** | Glucose | *T. hemsleyanum* *T. planicaule* | Rattan | Xu et al. (2014), Chen (2017) |
| **79** | Mannose | *T. hemsleyanum* | Root and leaf | Rao et al. (2016) |
| **80** | Rhamonse | *T.* hemsleyanum | Root and leaf | Rao et al. (2016) |
| **81** | *D*-Fructose | *T. hemsleyanum* | Leaf | Guo (2013) |
| **82** | Mannitol | *T. hemsleyanum*; *T. planicaule* | Aerial part, rattan | Liu (2000), Chen (2017) |
| **83** | RTP-1 | *T. hemsleyanum* | Root | Guo (2018) |
| **84** | RTP-2 | *T. hemsleyanum* | Root | Guo (2018) |
| **85** | RTP-3-1 | *T. hemsleyanum* | Root | Guo (2018) |
| **86** | TTP | *T. hemsleyanum* | Tuber | Chu et al. (2020) |
| **87** | THDP-3 | *T. hemsleyanum* | Leaf | Ru et al. (2019b) |
| **88** | TDGP-3 | *T. hemsleyanum* | Leaf | Ru et al. (2019a) |
| **89** | THP | *T. hemsleyanum* | Root | |
| **90** | THP | *T. hemsleyanum* | Leaf | Ru et al. (2018) |
| **91** | SYQP | *T. hemsleyanum* | Aerial part | Zhu et al. (2020) |
| **Terpenoids** | | | | |
| **92** | Taraxerone | *T. hemsleyanum*; *T. planicaule* | Aerial part; rattan | Liu (2000), Chen (2017) |
| **93** | Taraxerol | *T. hemsleyanum* | Aerial part | Liu (2000) |
| **94** | Oleanolic acid | *T. Hemsleyanum*; *T. planicaule* | Root tuber ; Rattan | Ding et al. (2015), Li (2020) |
| **95** | 3-*β*-(Stearyolxy) olean-12-ene | *T. planicaule* | Stem | Chen (2017) |
| **96** | Erythrodiol | *T. planicaule* | Rattan | Shao et al. (2010) |
| **97** | *α*-Amyrin | *T. hemsleyanum* | Aerial part | Liu (2000) |
| **98** | Ganoderic acid H | *T. hemsleyanum* | Root tuber | Sun (2018a) |
| **99** | Ioliolide | *T. erubescens* | Stem | Dao et al. (2014) |
| **100** | (+)-Dehydrovomifoliol | *T. erubescens* | Stem | Dao et al. (2014) |
| **101** | Pteroside Z | *T. hemsleyanum* | Aerial part | Sun (2018a) |
| **102** | Camphor | *T. hemsleyanum* | Tuber | Huo et al. (2008) |
| **103** | (4*R*,5*R*)-4-Hydroxy-2-methyl-5-propan-2-ylcyclohex-2-en-1-one | *T. hemsleyanum* | Tuber | Xu et al. (2017) |
| **104** | (4*S*,5*R*)-4-Hydroxy-2-methyl-5-propan-2-ylcyclohex-2-en-1-one | *T. hemsleyanum* | Tuber | Xu et al. (2017) |
| **105** | (4*R*,5*R*)-4-Hydroxy-5-isopropyl-2-methylcyclohex-2-enone | *T. hemsleyanum* | Tuber | Xu et al. (2017) |
| **Steroids** | | | | |
| **106** | *β*-Sitosterol | *T. hemsleyanum*; *T. planicaule*; *T. hypoglaucum* | Root tuber and aerial part; rattan; aerial part | Guo (2013), Liu (2000), Chen (2017) |
| **107** | Daucosterol | *T. hemsleyanum*; *T. planicaule*; *T. hypoglaucum* | Aerial part; rattan; aerial part | Liu (2000), Chen (2017) |
| **108** | *β*-Sitosteryl oleate | *T. planicaule* | Rattan | Chen (2017) |
| **109** | Daucosterol-6′-*O*-benzoyl | *T. hemsleyanum* | Root tuber | Sun (2018a) |
| **110** | 7*α*-Hydroxysitosterol | *T. planicaule* | Rattan | Shao (2011) |
| **112** | Ethyl 3*β*-hydroxy-5-cholen-26-oate | *T. planicaule* | Rattan | Chen (2017) |
| **113** | Ergosterol | *T. hemsleyanum* | Aerial part | Liu (2000) |
| **114** | 3*β*-Hydroxystigmast-5-en-7-one | *T. erubescens*; *T. planicaule* | Stem; Rattan | Dao et al. (2014), Li (2020) |
| **115** | Stigmast-4-ene-3*β*, 6*β*-diol | *T. erubescens* | Stem | Dao et al. (2014) |
| **116** | Stigmasterol | *T. planicaule, T. hemsleyanum* | Rattan Root tuber | Chen (2017), Sun et al. (2018) |
| **117** | (24*S*)-3*β*-Hydroxy-5*α*-stigmastan-6-one | *T. planicaule* | Rattan | Chen (2017) |
| **118** | Estigmast-4-en-6*β*-ol-3-one | *T. planicaule* | Rattan | Chen (2017) |
| **119** | Sitostane-3*β*, 5*α*, 6*β*-triol | *T. planicaule* | Rattan | Shao (2011) |
| **120** | 3*β*-Hydroxystiost-5-en-7-one | *T. planicaul* | Rattan | Shao (2011) |
| **121** | Stigmast-4,22-dien-3-one | *T. planicaule* | Rattan | Chen (2017) |
| **122** | Campesterol | *T. hemsleyanum* | Leaf | Sun (2018a) |
| **123** | *β*-Sitosterol palmitate | *T. planicaule* | Rattan | Chen (2017), Li (2020) |
| **124** | 3-Epipapyriferic acid | *T. hemsleyanum* | Root tuber | Sun (2018a) |
| **Phenylpropanoids** | | | | |
| **125** | Psoralene | *T. hemsleyanum* | Leaf | Sun (2018a) |
| **126** | Isoscopoletin | *T. planicaule* | Rattan | Chen (2017) |
| **127** | Dennettine | *T. planicaule* | Rattan | Chen (2017) |
| **128** | Bergenin | *T. erubescens* | Stem | Dao et al. (2014) |
| **129** | 3-*O*-Galloybergenin | *T. erubescens* | Stem | Dao et al. (2014) |

**Table 2** (*continued*)

| No. | Chemical names | Source plants | Distribution in plant | References |
|---|---|---|---|---|
| **130** | 1-Caffeoylquinic acid | *T. hemsleyanum* | Aerial part | Sun (2018a) |
| **131** | 5-*p*-Coumaroylquinic acid | *T. hemsleyanum* | Aerial part | Sun (2018a) |
| **132** | 1-*p*-Coumaroylquinic acid | *T. hemsleyanum* | Aerial part | Sun (2018a) |
| **133** | Neochlorogenic acid | *T. hemsleyanum* | Root tuber and aerial part | Xu et al. (2014), Fan et al. (2016) |
| **134** | Cryptochlorogenic acid | *T. hemsleyanum* | Root tuber; aerial part | Xu et al. (2014), Fan et al. (2016) |
| **135** | Coumaroylquinic acid | *T. hemsleyanum* | Leaf | Sun (2018a) |
| **136** | Feruloylquinic acid | *T. hemsleyanum* | Leaf | Sun et al. (2013) |
| **137** | Chlorogenic acid | *T. hemsleyanum* | Aerial part | Sun (2018a) |
| **138** | 5-Feruloylquinic acid | *T. hemsleyanum* | Aerial part | Sun (2018a) |
| **139** | 4-*p*-Coumaroylquinic acid | *T. hemsleyanum* | Root tuber | Chen (2014) |
| **140** | *p*-Coumaric acid | *T. hemsleyanum* | Aerial part | Sun (2018a) |
| **141** | Caffeic acid | *T. hemsleyanum* | Aerial part | Sun (2018a) |
| **142** | Cinnamic acid | *T. hemsleyanum* | Root tuber | Xu et al. (2017) |
| **143** | Ferulic acid hexoside | *T. hemsleyanum* | Aerial part | Sun (2018a) |
| **144** | 1-*O*-*trans*-*p*-Hydroxycinnamoyl-2′-*O*-*trans*-caffeoyl gentiobiose | *T. hemsleyanum* | Aerial part | Cai et al. (2018) |
| **145** | (+)-Lyoniresinol | *T. erubescens* | Stem | Dao et al. (2014) |
| **Alkaloids** | | | | |
| **146** | Indole | *T. hemsleyanum* | Aerial part | Wang et al. (2018) |
| **147** | Indole-3-carboxylic acid | *T. hemsleyanum* | Aerial part | Wang et al. (2018) |
| **148** | Indole-3-propanoic acid | *T. hemsleyanum* | Aerial part | Wang et al. (2018) |
| **149** | 5-Hydroxy-indole-3-carboxaldehyde | *T. hemsleyanum* | Aerial part | Wang et al. (2018) |
| **150** | 5-Hydroxy-indole-3-carboxylic acid | *T. hemsleyanum* | Aerial part | Wang et al. (2018) |
| **151** | 6-Hydroxy-3,4-dihydro-1-oxo-*β*-carboline | *T. hemsleyanum* | Aerial part | Wang et al. (2018) |
| **152** | Hippophamide | *T. hemsleyanum* | Aerial part | Wang et al. (2018) |
| **153** | Tetrastigmindole A | *T. obtectum* | Stem and leaf | Shi (2012) |
| **154** | Tetrastigmindole B | *T. obtectum* | Stem and leaf | Shi (2012) |
| **155** | *S*-(−)-Trolline | *T. hemsleyanum* | Aerial part | Wang et al. (2018) |
| **156** | Pyrrole-3-propanoic acid | *T. hemsleyanum* | Aerial part | Wang et al. (2018) |
| **157** | 4-Hydroxycinnamide | *T. hemsleyanum* | Aerial part | Wang et al. (2018) |
| **158** | Coelarthenol | *T. planicaule* | Rattan | Chen (2017) |
| **159** | Diphenylamine | *T. hemsleyanum* | Root tuber | Huo et al. (2008) |
| **Other compounds** | | | | |
| **160** | Linoleic acid | *T. hemsleyanum* | Root tuber and aerial part | Sun (2018a) |
| **161** | Palmitic acid | *T. hemsleyanum*; *T. planicaule*; *T. hypoglaucum, T. planicaule* | Root tuber; rattan; aerial part | Chen (2014), Shao (2011), Liu (2000) |
| **162** | Oleic acid | *T. hemsleyanum* | Root tuber | Ding et al. (2015) |
| **163** | *α*-Linolenic acid | *T. hemsleyanum* | Root tuber | Sun (2018a) |
| **164** | 9,12,15-Nonadecatrienoic acid | *T. hemsleyanum* | Root tuber | Hu et al. (2013) |
| **165** | Arachidic acid | *T. hemsleyanum* | Root tuber | Hu et al. (2013) |
| **166** | Dotriacontanoic acid | *T. hemsleyanum* | Aerial part | Liu (2000) |
| **167** | Lignoceric acid | *T. planicaule* | Stem | Chen (2017) |
| **168** | 9,12,15-Eicosatrienoic acid | *T. hemsleyanum* | Root tuber | Hu et al. (2013) |
| **169** | Myristic acid | *T. hemsleyanum* | Tuber | Sun (2018a) |
| **170** | Stearic acid | *T. hemsleyanum* | Root tuber | Sun (2018a) |
| **171** | Margaric acid | *T. planicaule* | Rattan | Chen (2017) |
| **172** | Caproic acid | *T. hemsleyanum* | Root tuber | Huo et al. (2008) |
| **173** | Pentadecylic acid | *T. hemsleyanum* | Root tuber | Huo et al. (2008) |
| **174** | Gheddic acid | *T. planicaule* | Whole plant | Li et al. (2014) |
| **175** | Succinic acid | *T. hemsleyanum*; *T. planicaule* | Aerial part; rattan | Liu (2000), Shao (2011) |
| **176** | (*Z*)-9,12,13-Trihydroxyoctadec-10-enoic acid | *T. hypoglaucum* | Aerial part | Liu (2000) |
| **177** | 9,12,15-Octadecatrienoic acid | *T. hemsleyanum* | Root tuber | Huo et al. (2008) |
| **178** | 6,10,14-Trimethyl-2-pentadecanone | *T. hemsleyanum* | Tuber | Huo et al. (2008) |
| **179** | Glyceryl monopalmitate | *T. planicaule* | Rattan | Chen (2017) |
| **180** | Azelaic acid | *T. hemsleyanum* | Root tuber | Sun (2018a) |
| **181** | Oxalic acid | *T. hemsleyanum* | Aerial part | Sun (2018a) |
| **182** | Pentacosane | *T. hypoglaucum* | Aerial part | Liu (2000) |
| **183** | Dodecanol | *T. planicaule* | Rattan | Chen (2017) |
| **184** | Tricosanol | *T. planicaule* | Whole plant | Li et al. (2014) |
| **185** | (*8,11R*,12R**,*9E*)-Trihydroxy-octadec-9-enoic acid | *T. planicaule* | Rattan | Shao (2011) |
| **186** | 12-Methyltridecan-1-ol | *T. planicaule* | Rattan | Chen (2017) |
| **187** | 2,3-Butanediol | *T. hemsleyanum* | Tuber | Huo et al. (2008) |
| **189** | 6,10,14-Trimethyl-2-pentadecanone | *T. hemsleyanum* | Tuber | Huo et al. (2008) |
| **190** | (9*R*)-Hydroxy-(10*E*,12*Z*,15*Z*)-octadecatrienoic-2′,3′-dihydroxypropyl ester | *T. hemsleyanum* | Root | Jin et al. (2018) |
| **191** | Citric acid | *T. hemsleyanum* | Root tuber and aerial part | Sun (2018a), Sun et al. (2018) |
| **192** | Fumaric acid | *T. hemsleyanum* | Aerial part | Sun (2018a) |
| **193** | Galactonic acid | *T. hemsleyanum* | Aerial part | Sun (2018a) |
| **194** | Malic acid | *T. hemsleyanum* | Aerial part | Sun (2018a) |
| **195** | Quinic acid | *T. hemsleyanum* | Root tuber | Sun (2018a) |
| **196** | Resveratrol | *T. hemsleyanum* *T. erubescens*; *T. hypogtaucum* | Root tuber; stem; aerial part | Chen (2014), Dao et al. (2014), Liu (2000) |

(*continued on next page*)

**Table 2** (*continued*)

| No. | Chemical names | Source plants | Distribution in plant | References |
|---|---|---|---|---|
| **197** | *trans*-Piceid | *T. hemsleyanum*; *T. erubescens* | Root tuber; stem | Guo (2013), Dao et al. (2014) |
| **198** | Astringin | *T. hemsleyanum* | Whole plant | Zeng (2013) |
| **199** | (*E*)2,3,5,4′-Tetrahydroxystilbene-2-*O*-*β*-*D*-Glucoside | *T. erubescens* | Stem | Dao et al. (2014) |
| **200** | Gallic acid | *T. hypoglaucum* | Aerial part | Liu (2000) |
| **201** | Ethyl gallate | *T. hemsleyanum*; *T. planicaul*; *T. hypoglaucum* | Whole plant; aerial part; Whole plant | Liu (2000), Li et al. (2014) |
| **202** | Salicylic acid | *T. hemsleyanum*; *T. planicaule* | Root tuber; rattan | Guo (2013), Chen (2017) |
| **203** | Benzoic acid | *T. hemsleyanum* | Root tuber | Fu et al. (2015) |
| **204** | Phenol | *T. hemsleyanum* | Root tuber | Huo et al. (2008) |
| **205** | Protocatechuic acid | *T. hemsleyanum*; *T. planicaule* | Root tuber; rattan | Chen (2014), Chen (2017) |
| **206** | *p*-Hydroxybenzoic acid | *T. hemsleyanum* | Leaf | Sun (2018a) |
| **207** | Vanillic acid | *T. erubescens*; *T. planicaule* | Stem; rattan | Dao et al. (2014), Chen (2017) |
| **208** | Syringic acid | *T. planicaule* | Rattan | Shao (2011) |
| **209** | Catechol | *T. hemsleyanum* | Root tuber | Zeng et al. (2017) |
| **210** | Protocatechualdehyde | *T. hemsleyanum* | Root tuber | Sun (2018a) |
| **211** | Vanillic acid-1-*O*-furan celery glucosyl ester | *T. hemsleyanum* | Root tuber | Zeng et al. (2017) |
| **212** | 1-*O*-galloyl-*β*-*D*-glucose | *T. hemsleyanum* | Aerial part | Sun et al. (2018) |
| **213** | 4-Hydroxy-3-methoxybenzaldehyde | *T. hemsleyanum*; *T. planicaule* | Root tuber; whole plant | Zeng et al. (2017), Ding et al. (2015) |
| **214** | Protocatechuic acid hexoside | *T. hemsleyanum* | Aerial part | Sun et al. (2018) |
| **215** | Glycerol-2-(3-methoxy-4-hydroxybenzoic acid) ether | *T. planicaule* | Rattan | Shao (2011) |
| **216** | Saccharumoside C/D | *T. hemsleyanum* | Root | Sun (2018a) |
| **217** | Tetrasigmol A | *T. erubescens* | Stem | Dao et al. (2014) |
| **218** | Apiosylglucosyl 4-hydroxybenzote | *T. hemsleyanum* | Root | Sun (2018a) |
| **219** | 4-Hydroxybenzoic acid | *T. hemsleyanum* | Root tuber | Chen (2014) |
| **220** | Cumene | *T. hemsleyanum* | Tuber | Huo et al. (2008) |
| **221** | Benzyl alcohol | *T. hemsleyanum* | Tuber | Huo et al. (2008) |
| **222** | 1′-*O*-Phenethyl-rutinose | *T. hemsleyanum* | Root tuber | Guo (2013) |
| **223** | Phenylethyl alcohol | *T. hemsleyanum* | Root tuber | Huo et al. (2008) |
| **224** | Emodin | *T. hemsleyanum* | Root tuber | Chen (2014) |
| **225** | Emodin-8-*O*-*β*-*D*-glucopyranoside | *T. hemsleyanum* | Root tuber | Chen (2014) |
| **226** | Physcione-8-*O*-*β*-*D*-glucopyranoside | *T. hemsleyanum* | Root tuber | Chen (2014) |
| **227** | Cyclotetraglutamipeptide | *T. hemsleyanum* | Aerial part | Liu (2000) |
| **228** | (4*R*,5*R*)-4-Hydroxy-5-isopropyl-2-methylcyclohex-2-enone | *T. hemsleyanum* | Root tuber | Xu et al. (2017) |
| **229** | 2*S*-Hydroxy-4-(4-hydroxyphenethoxy)-4-oxobutanoic acid | *T. hemsleyanum* | Aerial part | Cai et al. (2018) |
| **230** | Cerebroside | *T. planicaule* | Rattan | Li (2020) |
| **231** | 2-Carbonyl-*D*-gluconic acid | *T. hemsleyanum* | Root tuber | Hu et al. (2013) |
| **232** | 1-*O*-*β*-*D*-Glucopyranosyl-(2*S*, 3*S*, 4*R*, 8*E*)-2-N-[(2′*R*)-2′-hydroxydocosanoy]-3,4-dihydroxy-8-octadene(18) | *T. planicaule* | Rattan | Shao (2011) |
| **233** | 1-*O*-*β*-*D*-Glucopyranosyl-(2*S*, 3*S*, 4*R*, 8*E*)-2-N-[(2′*R*)-2′-hydroxytricosanoy]-3,4-dihydroxy-8-octadene(19) | *T. planicaule* | Rattan | Shao (2011) |
| **234** | 1-*O*-*β*-*D*-Glucopyranosyl-(2*S*, 3*S*, 4*R*, 8*E*)-2-N-[(2′*R*)-2′-hydroxytetracosanoy]-3,4-dihydroxy-8-octadene(20) | *T. planicaule* | Rattan | Shao (2011) |
| **235** | 1-*O*-*β*-*D*-Glucopyranosyl-(2*S*, 3*S*, 4*R*, 8*E*)-2-N-[(2′*R*)-2′-hydroxypentacosanoy]-3,4-dihydroxy-8-octadene(21) | *T. planicaule* | Rattan | Shao (2011) |
| **236** | 3,3′-Dimethoxy gallic acid-4-*O*-*β*-*D*-glucopyranoside | *T. hypoglaucum* | Aerial part | Liu (2000) |
| **237** | 3,3′-Dimethoxy gallic acid-4-*O*-*β*-*D*-xylopyranside | *T. hypoglaucum* | Aerial part | Liu (2000) |
| **238** | cerebroside | *T. planicaule* | Rattan | Li (2020) |
| **239** | 2-Methoxy-4-methylbenzene-1-*O*-furacresyl glucoside | *T. hemsleyanum* | Root tuber | Zeng et al. (2017) |
| **240** | *p*-Hydroxybenzaldehyde | *T. hemsleyanum* | Leaf | Sun (2018) |
| **241** | 1-*O*-*trans*-*p*-Hydroxycinnamoyl-2′-*O*-*trans*-caffeoyl gentiobiose | *T. hemsleyanum* | Aerial part | Cai et al. (2018) |
| **242** | (3*R*,4*S*,5*R*)-3,4-Dihydroxy-5-(*R*)-1-hydroxyeicosyl) dihydrofuran-2(3*H*)-one | *T. hemsleyanum* | Aerial part | Cai et al. (2018) |
| **243** | (4*R*,5*R*)-4-Hydroxy-5-isopropyl-2-methylcyclohex-2-enone | *T. hemsleyanum* | Root tuber | Xu et al. (2017) |
| **244** | 9-Hydroxy-10,12-dienoic acid | *T. hemsleyanum* | Root tuber | Xu et al. (2017) |
| **245** | 9(9*R*)-Hydroxy-(10*E*,12*Z*,15*Z*)-octadecatrienoic-2′,3′ -dihydroxypropyl ester | *T. hemsleyanum* | Root | Jin et al. (2018) |
| **246** | (4*R*,5*R*)-4-Hydroxy-2-methyl-5-propan-2-ylcyclohex-2-en-1-one | *T. hemsleyanum* | Root tuber | Xu et al. (2017) |
| **247** | (4*S*,5*R*)-4-Hydroxy-2-methyl-5-propan-2-ylcyclohex-2-en-1-one | *T. hemsleyanum* | Root tuber | Xu et al. (2017) |
| **248** | (3*R*,4*R*,6*S*)-3,6-Dihydroxy-1-menthene | *T. hemsleyanum* | Root tuber | Xu et al. (2017) |

So far, eight monosaccharides (**75**–**82**) and nine polysaccharides (**83**–**91**) were reported in *T. hemsleyanum*, only two monosaccharides (**78** and **82)** were reported in *T. planicaule*, and no saccharide was reported in other medicinal plants. The polysaccharide RTP-1 (**83**) and RTP-2 (**84**) were isolated successively from roots of *T. hemsleyanum*. Moreover, further study showed that the high purity polysaccharide RTP-3-1 (Guo, 2018) (**85**) with a molecular weight of 1244.2 kDa mainly consists of four kinds of monosaccharide:

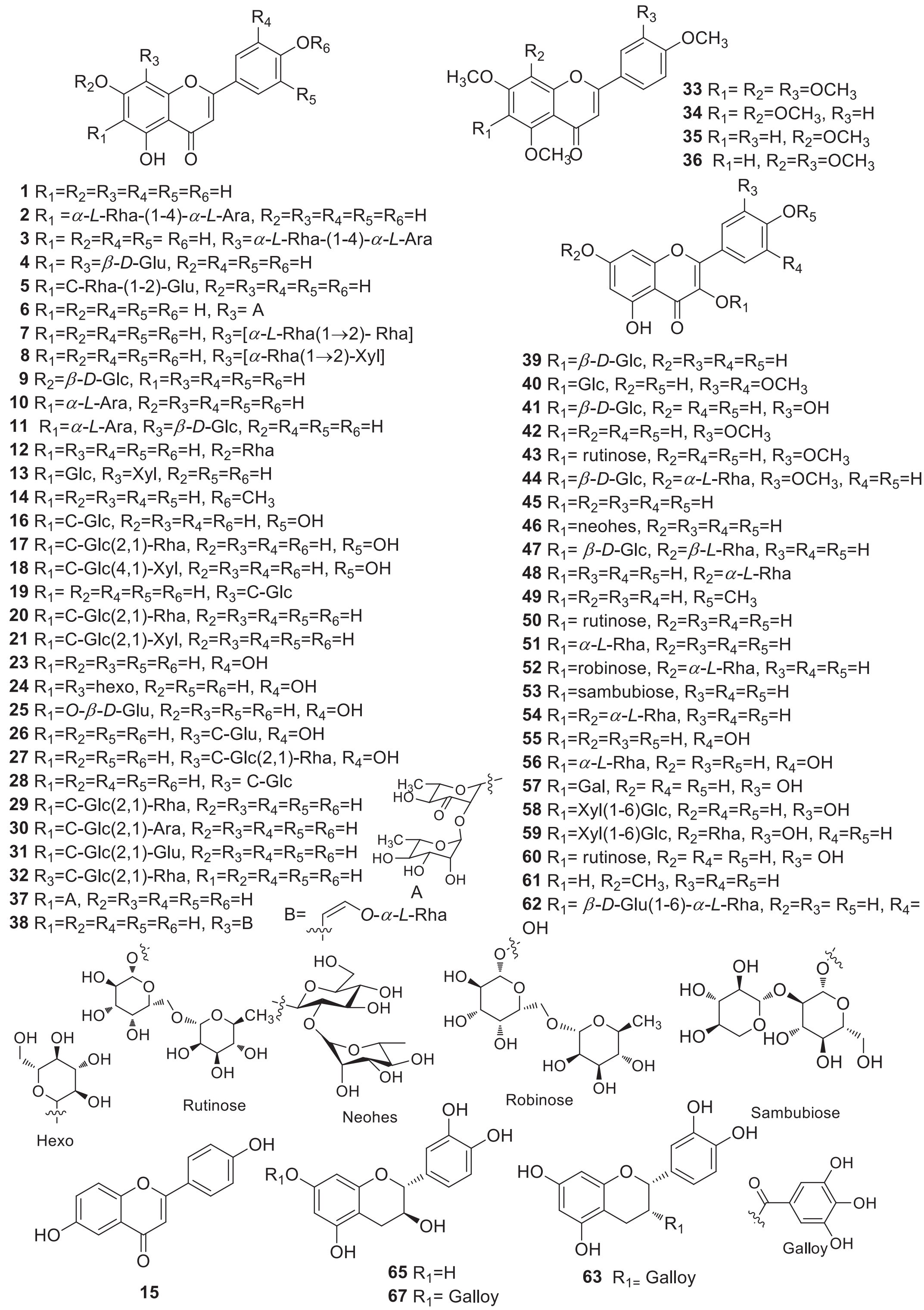


**Fig. 2.** Chemical structures of flavonoids isolated from genus *Tetrastigma*.

arabinose, galacturonic acid, galactose, and fructose and they account for 8.39%, 7.18%, 20.70%, and 63.70%, respectively. TTP-1 (**86**) (Chu et al., 2019) was a purified polysaccharide extracted from tuber of *T. hemsleyanum* with the average molecular weight of 478.33 kDa that was composed of 38.91% mannose, 14.87% glucuronic acid, 1.31% galacturonic acid, 42.81% galactose, and 2.1% arabinose. A novel polysaccharide named TDGP-3 (Ru et al., 2019a) (**88**) was extracted from leaves of *T. hemsleyanum* with a molecular weight of 3.31 $\times$ $10^5$ Da, which was composed of 1,4-Glcp, 1,4-Glap and 1,3,6-Manp linkage in the main chain. Mean-

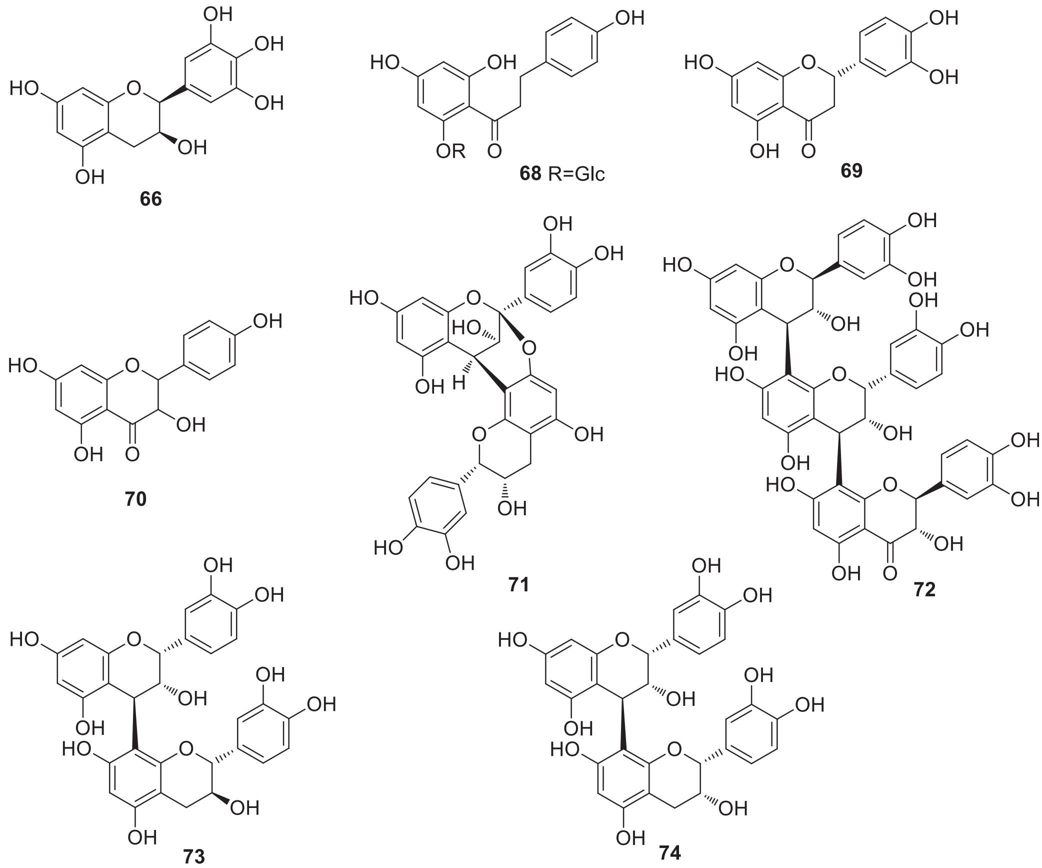


**Fig. 2** (*continued*)

while, a novel polysaccharide THDP-3 (Ru et al., 2019b) (**87**) was found in cane leaves of *T. hemsleyanum* with a molecular weight of 77.98 kDa that consists of rhamnose, arabinose, mannose, glucose, galactose and their ratio is 1.0:1.3:2.5:2.3:3.1 with main backbones of → 4)-α-*D*-GalAp-(1→,→4)-*β*-*D*-Galp-(1 → and → 4)-α-*D*-Glcp-(1→, and main branches of *β*-*D*-Manp-(1→, →3,6-*β*-*D*-Manp-1 → and α-*D*-Araf-(1→. A water-soluble polysaccharide named THP (Ru et al., 2018) (**89**) with a molecular weight of 93307 Da is composed of rhamnose, arabinose, mannose, glucose, galactose in the molar ratio of 0.07:0.14:0.38:0.21:0.31. SYQP (Zhu et al., 2020) (**91**) was a purified polysaccharide extracted from the aerial part of *T. hemsleyanum* with an average molecular weight of 66.2 kDa that consists of galacturonic acid, glucose, mannose, arabinose, galactose, and rhamnose with a molar ratio of 11.3:7.1:2.5:1.0:0.9:0.5. The names and sources of these compounds are shown in Table 2, and the structures are shown in Fig. 3.

### 3.3. Terpenoids

So far, there are 14 terpenoids isolated from *Tetrastigma* species, including seven triterpenoids (**92–98**) and seven others (**99–105**). Triterpenoids isolated from *Tetrastigma* species can be divided into three types for their different skeletons: oleanane-type (**92–96**), lanostane-type (**98**) and ursane-type (**97**). Among them, **92–94**, **97** and **98** were isolated from aerial parts of *T. hemsleyanum*. Compounds **92, 95** and **96** were obtained from the stem of *T. planicaule*. Other terpenoids were monoterpenes and sesquiterpenes. One sesquiterpene (**101**) and four monoterpenes (**102–105**) were isolated from *T. hemsleyanum*. In particular, there were two norisoprenoids (**99–100**) that were found in the stem of *T. erubescens*. The names and sources of these compounds are shown in Table 2, and the structures are shown in Fig. 4.

### 3.4. Steroids

Steroids are another type of bioactive constituent in *Tetrastigma* species. Steroids are secondary metabolites formed by cyclopentano-perhydrophenthrene with four ring systems (6/6/6/5) in their basic skeleton. To date, 19 steroids were identified in the genus *Tetrastigma* and they were sterols and mainly found in *T. planicaule* and *T. hemsleyanu*m. The names and sources of these compounds are shown in Table 2, and the structures are shown in Fig. 5.

### 3.5. Phenylpropanoids

At present, phytochemical studies led to the isolation and identification of 21 phenylpropanoids from the *Tetrastigma* species. According to the structure characteristics, they can be divided into two types: coumarins (**125–144**), and lignans (**145**). Two coumarins (**125–126**) and one lignan (**145**) were obtained from the stem of *T. erubescens.* Two coumarins (**126–127**) were isolated from the stems of *T. planicaule*. In fact, almost all phenylpropanoids were

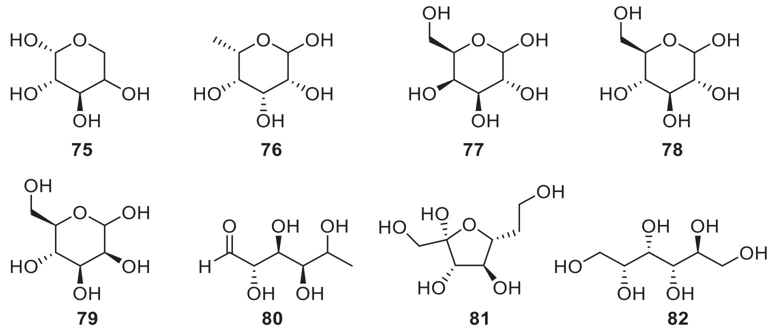


**Fig. 3.** Chemical structures of monosaccharides isolated from genus *Tetrastigma*.

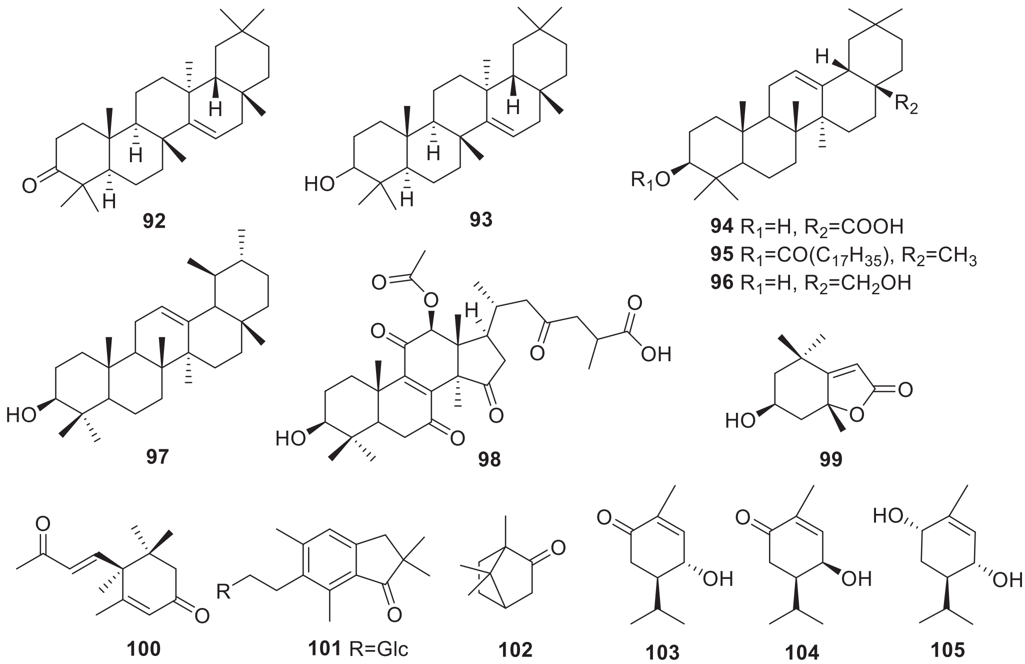


**Fig. 4.** Chemical structures of terpenoids isolated from genus *Tetrastigma*.

found in *T. hemsleyanum*, and **130**–**139** were isomers and derivatives of chlorogenic acid (**137**). The names and sources of these compounds are shown in Table 2, and the structures are shown in Fig. 6.

### 3.6. Alkaloids

Alkaloids are also important active ingredients in this genus and they are mainly indole alkaloids. At present, 14 alkaloids were reported from this genus, including nine indole alkaloids (**146**–**154**) and five other alkaloids (**155**–**159**). Indole alkaloids: tetrastigmindole A (**153**) and tetrastigmindole B (**154**) (Shi, 2012) were new secondary metabolites isolated from *T. obtectum*. Seven indole alkaloids (**146**–**151** and **153**), an amide (**156**), a maleimide (**155**) and a carboline (**157**) were isolated from the aerial parts of *T. hemsleyanum*, and they were alkaloids isolated from the genus *Tetrastigma* firstly. Furthermore, structure–activity relationship (SAR) studies showed that the lactam moiety may be an important structural element for their anti-inflammatory activity. Only one alkaloid, coelarthenol (**158**) (Chen, 2017), was isolated from *T. planicaule*. The names and sources of these compounds are shown in Table 2, and the structures are shown in Fig. 7.

### 3.7. Other compounds

Aliphatics, phenolic acids and other compounds also presented abundantly in this genus, **160**–**194** are long chain fatty acids and **196**–**223** are phenolic acids. **196**–**199** were derivatives of resveratrol (**196**), **224**–**226** were anthraquinones, while **227**–**235** were other compounds. The names and sources of these compounds are shown in Table 2, and the structures of representative compounds are shown in Fig. 8.

## 4. Pharmacological activities

The extracts and compounds of *Tetrastigma* species showed various biological activities including antitumor, antipyretic and analgesic, antiviral, hepatoprotective and antidiabetic properties. These bioactivities are summarized below.

### 4.1. Antitumor activity

#### 4.1.1. Antitumor activity of plant extracts

Antitumor activity of the ethyl acetate extract of *T. hemsleyanum* was investigated by establishing colorectal cancer with

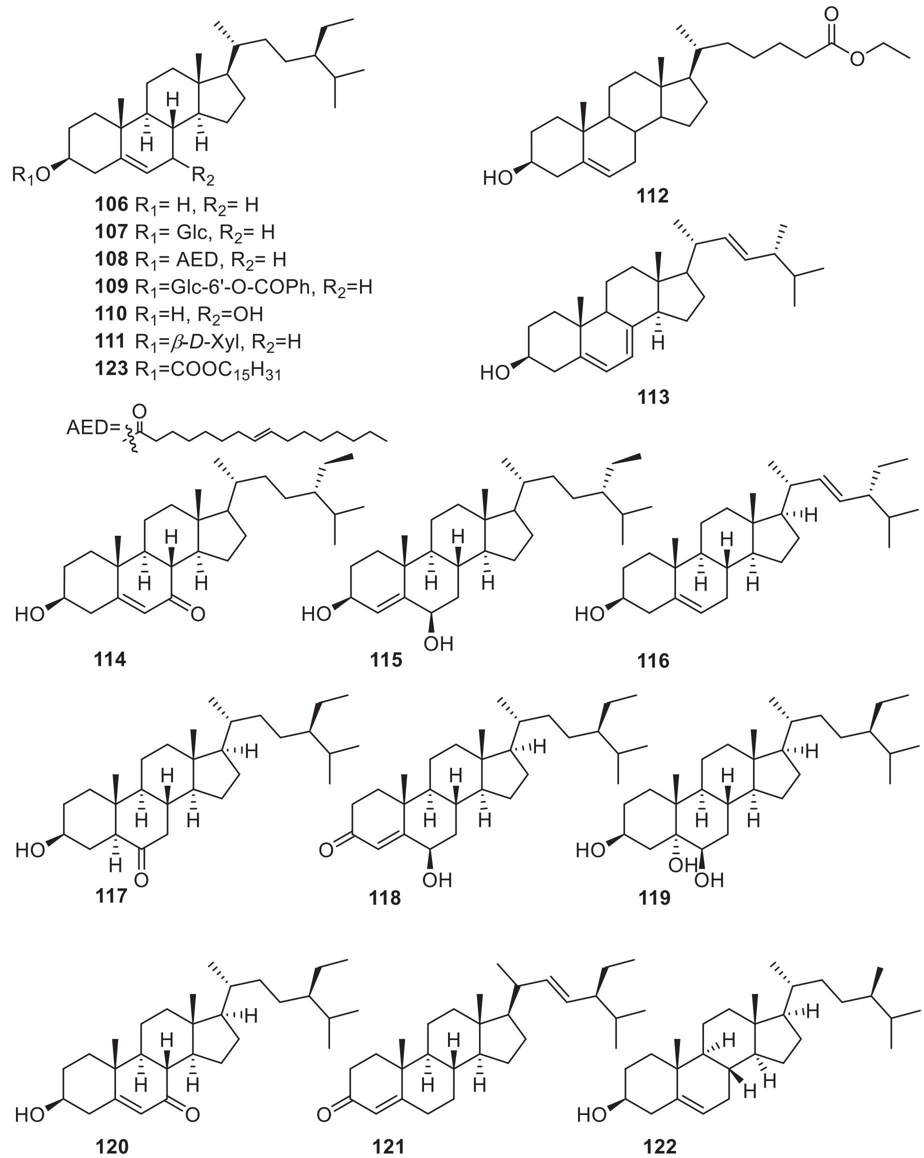


**Fig. 5.** Chemical structures of steroids isolated from genus *Tetrastigma*.

HT29 cells model in mice. The extract could inhibit the growth of subcutaneous transplanted tumor of colon cancer HT29. The possible mechanism was related to up-regulation of the expression of Caspase-3 protein and induction of the apoptosis of subcutaneous transplanted tumor of colon cancer HT29 cells (Lin et al., 2016). The water extract of *T. hemsleyanum* was explored for their antitumor activity by CCK8 (Cell Counting Kit-8) assay and flow cytometry (FCM) *in vitro*. The result showed the water extract of *T. hemsleyanum* not only promoted the proliferation of NK (Natural Killer cell), but also enhanced the cytotoxic activity of NK cells against gastric cancer cell lines BGC-823. The possible mechanism may be that the water extract of *T. hemsleyanum* could increase expressions of perforin (PFP), Granzyme (GraB) and CD107a (Yuan et al., 2016). The water extract and diethyl ether extract of *T. hemsleyanum* displayed definite antitumor activity *in vitro*, and their $IC_{50}$ were 99.7 μg/mL and 127.8 μg/mL, respectively. (Chen, 2014). The water, ethanol and ethyl acetate extracts of *T. hemsleyanum* displayed inhibitory effects on the growth of breast cancer cells MCF-7 *in vitro* ($p < 0.05$). All extracts could promote the apoptosis of MCF-7 cells and their apoptotic rates were (15.60 ± 4.03)%, (17.32 ± 3.87)% and (29.45 ± 6.19)%, respectively (Qiu et al., 2018). Polysaccharides from aerial part of *T. hemsleyanum* showed significant antitumor activity in inhibiting tumor growth and distal lung metastasis explored by establishing breast cancer with 4T1 cells model in mice. The result showed the tumor inhibition rates of low, middle and high dose polysaccharides were 25.09%, 28.79% and 34.21%, respectively (Guo et al., 2019). Cytotoxicity of RTP (polysaccharides extracted from roots of *T. hemsleyanum*) was tested by MTT assay. It was found that RTP could induce human gastric cancer cell apoptosis in dose-dependent manner, the apoptotic rates at the concentration of 0.625 mg/mL, 1.25 mg/mL and 2.5 mg/mL were 24.97%, 58.35% and 81.46%, respectively (Guo,

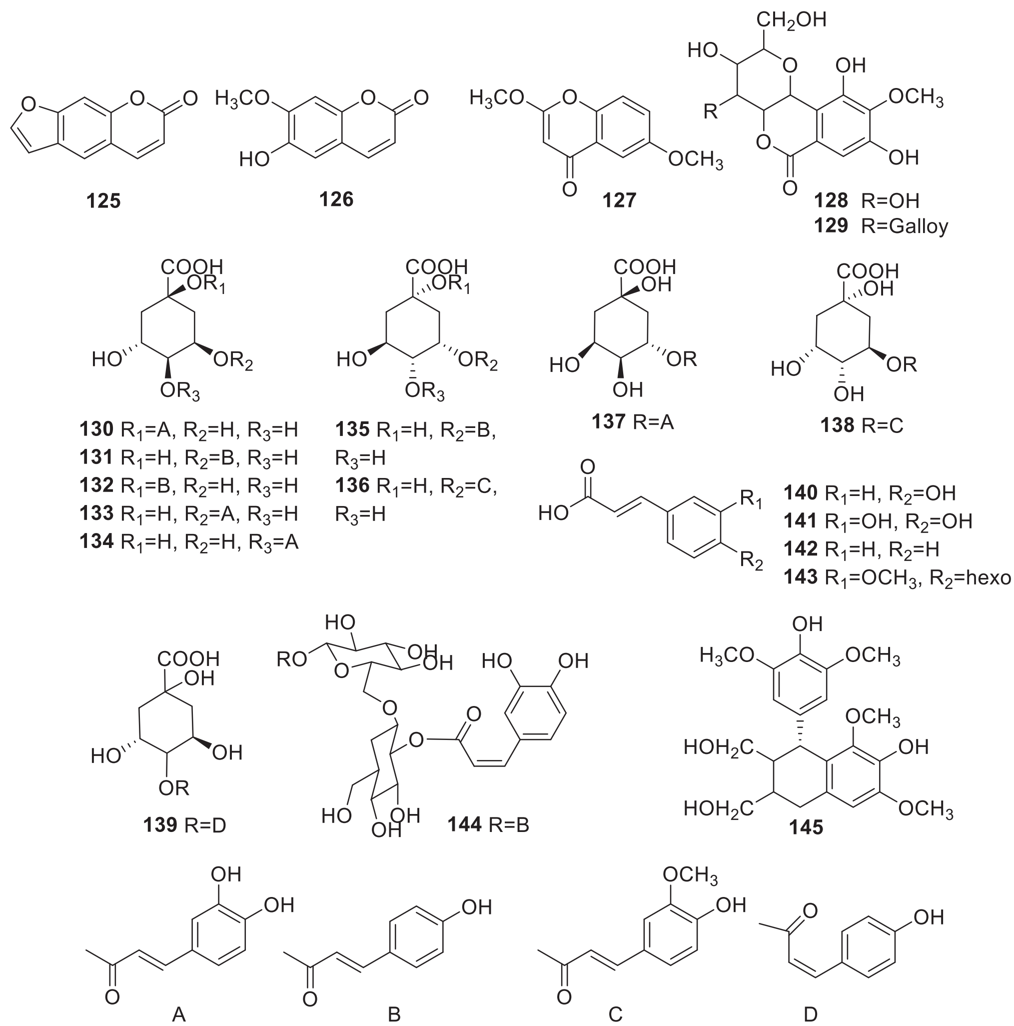

Fig. 6. Chemical structures of phenylpropanoids isolated from genus *Tetrastigma*.

2018). The antitumor activity of flavonoid extracts of *T. hemsleyanum* were investigated by establishing Lewis lung carcinoma model in mice. The result showed the flavonoid extracts could decrease prostaglandin 2 (PGE2) and cyclooxygenase-2 (COX-2) in a dose-dependent manner. The possible mechanism may be related to regulation of the expression of PGE2 and COX-2 (Zhang and Feng, 2019). Antitumor activity of flavonoid extract of *T. hemsleyanum* was researched by microRNA sequencing (miRNA-seq) and bioinformatics technology. The result showed that the flavonoid extract of *T. hemsleyanum* could inhibit the proliferation and invasion of lung cancer cell line A549, and induce its apoptosis (Wei et al., 2018). The flavonoid extract of *T. hemsleyanum* had a significant inhibitory effect on the proliferation of non-small cell lung cancer A549 cells in a dose-dependent manner. The mechanism may be related to the regulation of ubiquitin–proteasome pathway (Zhong et al., 2017). The ethyl acetate extract of *T. hemsleyanum* showed antitumor activity by inhibiting the subcutaneous transplanted tumor of HepG-2 without dose-dependent. The mechanism may be related to the increase of the levels of serum TNF-$\alpha$ and IFN-$\gamma$ (Wang et al., 2014). The ethyl acetate extracts of *T. hemsleyanum* could induce apoptosis of human liver cancer HCCC-9810 cells with a dose-dependent and time-dependent inhibitory (Wang & Peng, 2015) and its $IC_{50}$ of treatment for 24 h, 48 h and 72 h were 275.3 mg/L, 183.3 mg/L and 75.8 mg/L, respectively. The possible mechanism was based on activation of the mitochondrial apoptotic pathway. Through MTT method, it was found the petroleum ether and *n*-butanol extracts of *T. planicaule* showed significant antitumor activity by inhibiting the growth of liver cancer HepG-2 cells (Chen, 2017). The flavonoid extract of *T. hemsleyanum* showed antitumor effect, and the possible mechanism was related to the down-regulation of MDSCs (myeloid-derived suppressor cells), COX-2 and PGE2 (Hu et al., 2021). The flavonoid extract of *T. hemsleyanum* showed antitumor activity in inhibiting proliferation and promoting apoptosis of bladder cancer cells through STAT3 signaling pathway (Wu, 2021). The flavonoid extract of *T. hemsleyanum* showed antitumor activity in reducing the proportion of Treg cells in Lewis lung cancer mice, improving the cellular immune function, and inducing the apoptosis of transplanted tumor tissues (Lin et al., 2021).

The polysaccharides from roots of *T. hemsleyanum* were explored for their antitumor activity by MTT methods. The result showed the polysaccharides could inhibit the proliferation, migration and invasion of hepatocellular carcinoma HepG2 cells and induce apoptosis. The mechanism may be related to the down-

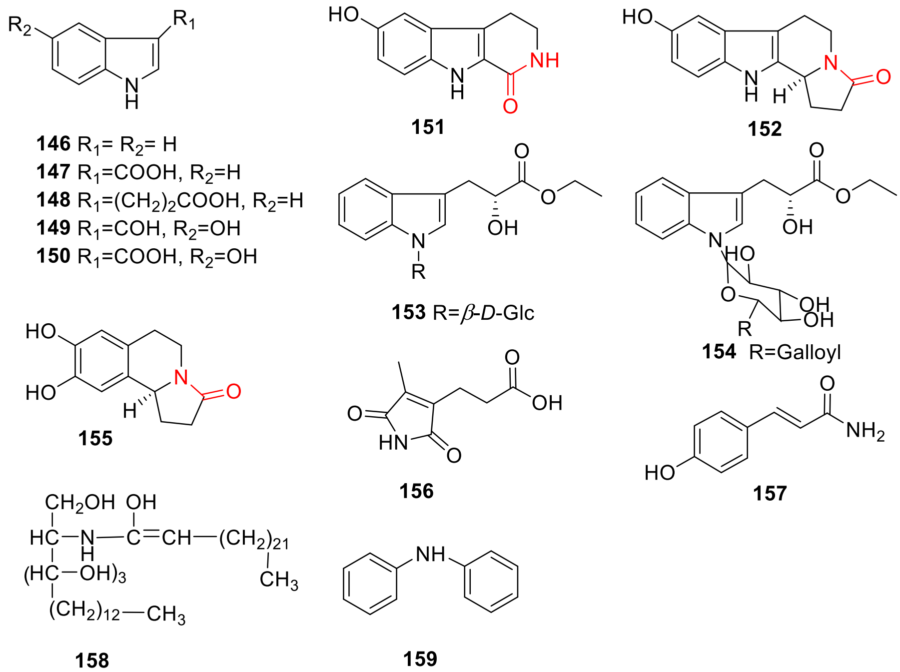


**Fig. 7.** Chemical structures of alkaloids isolated from genus *Tetrastigma*.

regulation of miR-151 expression (Wang et al., 2020). The flavonoid extract of *T. hemsleyanum* showed antitumor activity in inhibiting the proliferation and invasion of breast cancer cells MCF-7. The possible mechanism may be related to blockage of the cell cycle in $G_0/G_1$ phase and regulation of the expression of proteins related to Wnt/β-catenin signaling pathway (Du et al., 2020). The ethanol extract of *T. hemsleyanum* had inhibitory effect on the proliferation of Hela cells. At the concentration of 8 mg/mL, the inhibition rates were 38.4% and 47.2% after incubation for 24 h and 48 h, respectively (Huang et al., 2020). The polysaccharides from the roots of *T. hemsleyanum* could inhibit the proliferation, migration and invasion of liver cancer cells, and induce cell apoptosis by down-regulating the expression of miR-151 (Wang, 2020). The flavonoid extract of *T. hemsleyanum* had an inhibitory effect on the proliferation of breast cancer cells MCF-7, MDA-MB-468, 4T1 and T47D by inhibiting the expression of p-p42/44, blocking the MAPK signaling pathway, and activating the apoptosis-related protein Caspase-3. (Qiu et al., 2019).

### 4.1.2. Antitumor activity of monomeric compounds

Apigenin (**1**) from *T. hemsleyanum* exhibited significant antitumor activity and its $IC_{50}$ values for HepG2 (human hepatocarcinoma), HCT-8 (human colon) and A549 (human lung adenocarcinoma epithelial) cells were (73.16 ± 0.96), (45.04 ± 1.25) and (48.66 ± 1.56) μg/mL, respectively (Lin et al., 2015). β-Sitosterol (**106**) and oleanolic acid (**94**) from *T. hemsleyanum* showed strong cytotoxic activity against Hela 229 (human cervical cancer cells) with $IC_{50}$ of 40.78 and 25.69 μg/mL, respectively. Furthermore, oleanolic acid had strong cytotoxic activity to A375 with an $IC_{50}$ of 69.87 μg/mL (Ding et al., 2015). Resveratrol (**196**) and kaempferol (**45**) displayed significant antitumor activities, and their $IC_{50}$ were 92.4 and 294.2 μg/mL (Chen, 2014), respectively. Tetrastigmindole A (**153**) and tetrastigmindole B (**154**) from *T. obtectum* showed positive effects on antitumor metastasis in MDA-MB-231 cell lines (human breast cancer cell lines) at a concentration of 20 μg/mL. The value of inhibition ratio on MDA-MB-23 cells were 70.3% and 59.2%, respectively (Shi, 2012; Zhao et al., 2020). Astragalin (**39**), isoquercitrin (**41**), kaempferol-3-rutinoside (**50**), rutin (**62**) and catechin (**65**) from *T. hemsleyanum* exhibited potential antitumor activity against HepG2 with $IC_{50}$ of (592.12 ± 3.31) μg/mL, (403.26 ± 1.26) μg/mL, (389.71 ± 4.23) μg/mL, (312.23 ± 1.17) μg/mL and (218.31 ± 2.38) μg/mL, respectively (Sun et al., 2015). *p*-Hydroxybenzoic acid (**206**) from *T. hemsleyanum* exhibited obvious inhibitory effects on MDA-MB-435S cell lines with $IC_{50}$ value of (92.39 ± 1.68) μg/mL (Lin et al., 2016). Procyanidins B1 (**73**) and catechin (**65**) were antitumor angiogenesis active ingredient of *T. hemsleyanum*, which could reduce the activity of vascular endothelial growth factor (VEGF) to inhibit cell migration, invasion and tubular formation ability, and repress the expression of MAPK/ERK, PI3K/AKT pathway to inhibit tumor angiogenesis (Sun, 2018b).

### 4.2. Antioxidant activity

Tetrasigmol A (**217**), catechin (**63**), epicatechin-3-*O*-gallate (**65**), phlorizin (**68**), 3-*O*-galloybergenin (**129**), resveratrol (**196**), (*E*)-2,3,5,4′-Tetrahydroxystilbene-2-*O*-*β*-*D*-glucoside(**199**), (+)-lyoniresinol (**145**) isolated from the stems of *T. erubescens* showed more potent antioxidant activities, with $IC_{50}$ values in the range of 1.8–60.4 μmol/L. Catechin (**65**), epicatechin-3-*O*-gallate (**63**) and 3-*O*-galloyberrgenin (**129**) exhibited much higher activity than the positive control trolox ($IC_{50}$ = 7.0 μmol/L) with $IC_{50}$ of 5.4, 2.2 and 1.8 μmol/L (Dao et al., 2014), respectively. *In vitro* models explicitly disclosed that the polysaccharides (THP) obtained from roots of *T. hemsleyanum* could protect RAW264.7 cells against $H_2O_2$ induced cytotoxicity by decreasing intracellular ROS levels,

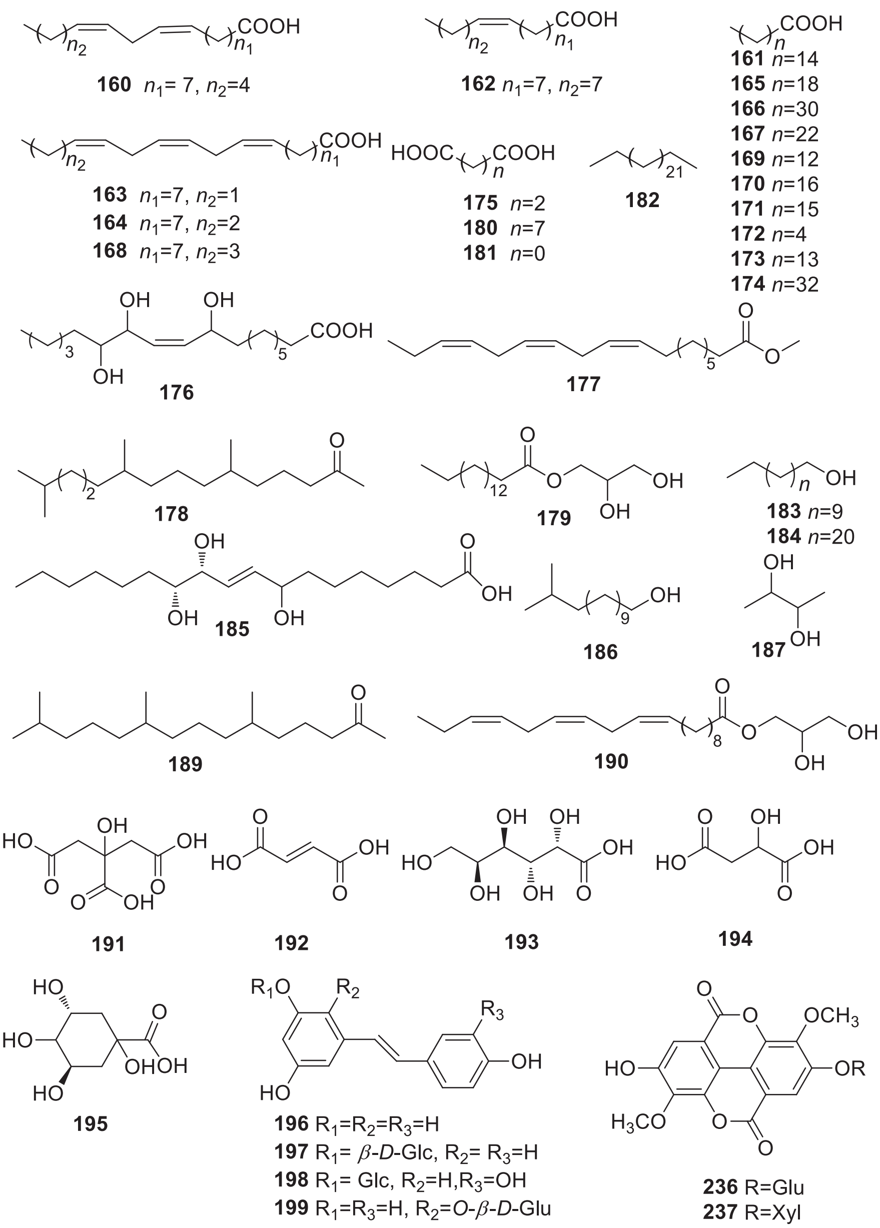


**Fig. 8.** Chemical structures of other compounds isolated from genus *Tetrastigma*.

reducing catalase (CAT) and superoxide dismutase (SOD) activities, increasing lactate dehydrogenase (LDH) activity and enhancing malondialdehyde (MDA) level (Huang et al., 2021). $Fe^{3+}$ reduction/antioxidant ability of the different extracts (total extract, petroleum layer, ethyl acetate layer, n-butanol layer, water layer) from *T. planicaule* was weaker than vitamin C (VC), but higher than tea polyphenols except water layer, and OH· scavenging activity of ethyl acetate layer ($IC_{50}$ = 0.028 g/L) was higher than $V_C$ ($IC_{50}$ = 0.044 g/L) and tea polyphenols ($IC_{50}$ = 0.032 g/L) (Pan et al., 2013). *T. planicaule* exhibited a good antioxidant capacity, which may be attributed to the total flavonoid content (Pan et al., 2012). The extracts of the root tuber and aerial part from *T. hemsleyanum* had certain scavenging ability to 2,2-diphenyl-1-picrylhydrazyl (DPPH) free radicals. When the DPPH scavenging rate of root tuber and aerial part reaches 50%, the required effective concentrations are 0.1902 and 0.1395 mg/L, respectively (Zhang et al., 2021). The soluble polysaccharide extracted by water from *T. hemsleyanum* showed antioxidant activity. The total antioxidant activity unit was 88.96 U·mL/L. The scavenging rates of DPPH, hydroxyl and superoxide anion radical were 36.8%, 65.1% and 36.8%, respectively (Yin et al., 2020).

### 4.3. Anti-inflammatory and analgesic activity

Hydroxy-3,4-dihydro-1-oxo-*β*-carboline (**151**), hippophamide (**152**) and *S*-(-)-trolline (**155**) from the aerial parts of *T. hemsleyanum* showed potent inhibitory activity against lipopolysaccharide (LPS)-stimulated NO production in RAW264.7 cells with $IC_{50}$

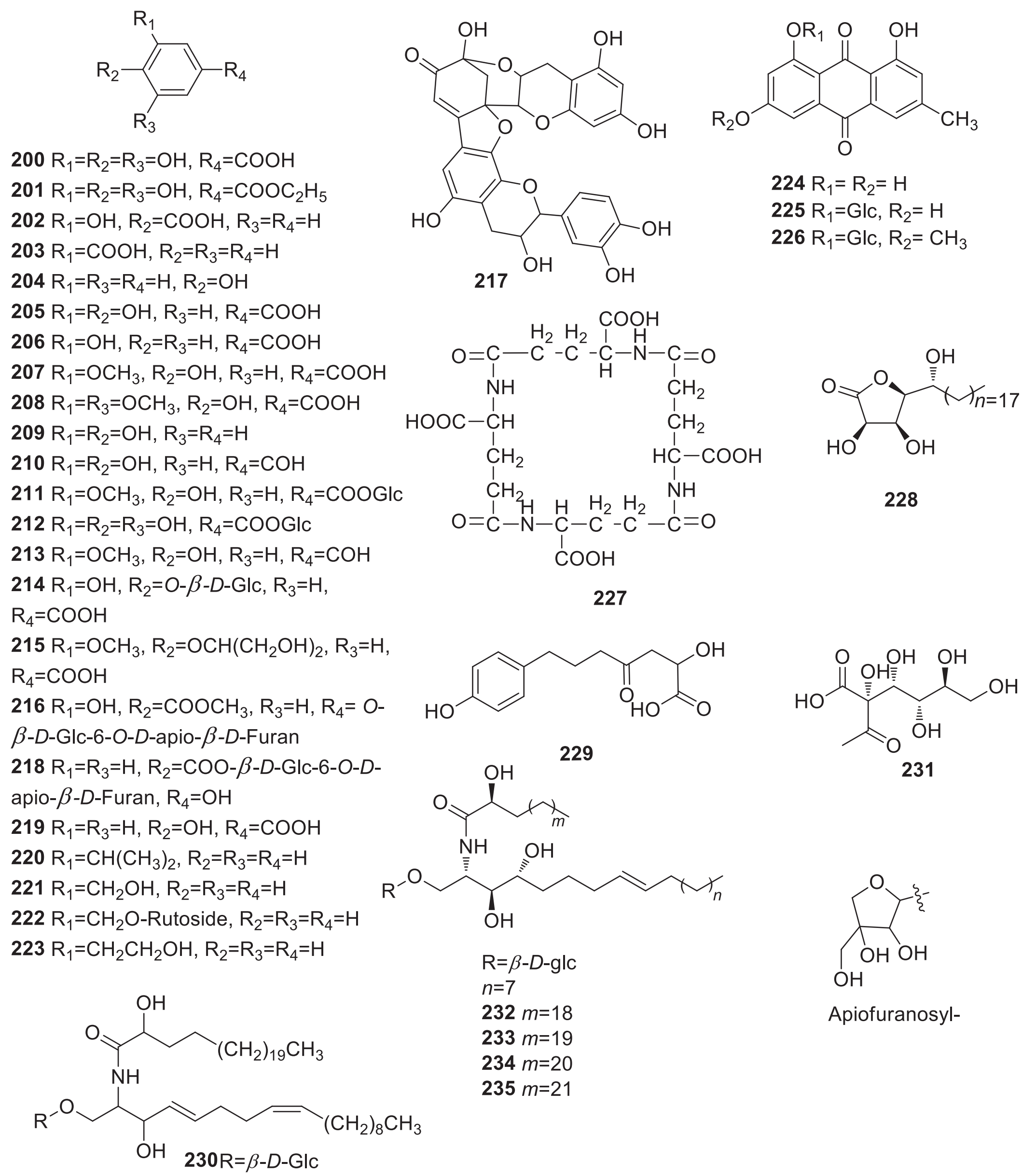


**Fig. 8** (*continued*)

of 31.9, 25.2 and 6.3 μmol/L, respectively. Among them, *S*-(-)-trolline (**155**) showed anti-inflammatory activity by inhibiting the activation of NF-κB (nuclear factor κB) and ERK-MAPK (extracellular signal-regulated protein kinase)-MAPK (mitogen-activated protein kinase) signaling pathway in RAW264.7 cells stimulated by LPS in a dose-dependent manner (Wang et al., 2018). Furthermore, structure–activity relationship (SAR) studies showed the lactam moiety may be an important structural element for their anti-inflammatory activity. Polysaccharide extracted from *T. hemsleyanum* can significantly inhibit the death of RAW264.7 cells induced by LPS, and the contents of TNF-α and IL-6 in RAW264.7 cells were significantly decreased compared with the model group in a dose-dependent manner (Huang, 2017). The extract of *T. planicaule* had an inhibitory effect on the degradation of IκB-α induced by TNF-α, and it was found that the extract could also inhibit the transport of NF-κB to the nucleus (Zhao et al., 1999). In the experiment of xylene ear swelling model and the acetic acid writhing in mice, *T. hypoglaucum* extract showed a significant inhibitory effect on ear swelling and writhing in mice (Li et al., 2018). The water extract of *T. hemsleyanum* showed a good anti-inflammatory effect in COPD copied by being smoked and LPS in rat model. Compared with the model group, the contents of TNF-α and IL-1β and the total number of leukocytes and neutrophils in experimental groups were significantly decreased in a dose-dependent manner (Jiang et al., 2018). The flavonoid extract of *T. hemsleyanum* significantly reduced the number of leukocyte and neutrophils infiltration in bronchoalveolar lavage fluid (BALF) ($p < 0.01$), inhibited secretion of IL-1β, IL-6, IL-12p40, TNF-α and sTNF-R1 ($p < 0.01$), improved the pathological damage of lung tissue, and significantly attenuated the phosphorylation of p38MAPK, NF-κB and the DNA binding activity of NF-κB in lung tissue ($p < 0.01$) (Liu et al., 2015). Kaempferol-3-*O*-rutinoside (**50**), isoquercitrin (**41**), rutin (**62**) in roots and vitexin (**28**) and orientin (**26**) in leaves from *T. hemsleyanum* showed anti-inflammatory activity by interacting with Keap1 protein and activating Nrf2 (Xing et al., 2020). TTP-1 (**86**) from *T. hemsleyanum* could suppress inflammation by attenuating inflammation via COX-2, iNOS, MAPKs pathways. Meanwhile, TTP could ameliorate oxidative damage through Nrf2-Keap1, Sirt1-FoxO1 pathways in RAW264.7 cells *in vitro* (Chu et al., 2020). Kaempferol rutinoside (**50**), isoquercitrin (**41**), rutin (**62**), vitexin (**28**) and orientin (**26**) from *T. hemsleyanum* could reduce the protein levels of pro-inflammatory cytokines, such as IL-6 and IL-1β. Furthermore, vitexin (**28**) had the strongest antiinflammatory which mechanism was related to directly binds with Keap1 to block Keap1-Nrf2 interaction to activate Nrf2, and thereby inhibiting gene and protein expression of pro-inflammatory cytokines (Xing, 2020).

### 4.4. Hepatoprotective activity

Li et al. (2018) used ANIT (α-isothiocyanatoacetate) to replicate the acute jaundice hepatitis model that caused liver damage in mice and found that the alcohol extract of *T. hemsleyanum* had a protective effect on liver damage. The mechanism of action was likely through reducing the production of inflammatory factors, promoting the metabolism of total bilirubin, and reducing the degree of lipid peroxidation. The alcohol extract of *T. planicaule* had a remarkable protective effect against liver injury by resisting the increase of serum aspartate transaminase (AST) ($p < 0.01$) and alanine transaminase (ALT) ($p < 0.01$) in mice with acute liver injury caused by $CCl_4$, down-regulating the content of malondialdehyde (MDA) ($p < 0.01$) in liver homogenate, enhancing the activity of superoxide dismutase (SOD) ($p < 0.01$), and significantly improving the pathological changes of liver tissue (Bin et al., 2016).

### 4.5. Antidiabetic activity

A novel polysaccharide THDP-3 (**87**) purified from cane leaves of *T. hemsleyanum* exhibited significant hypoglycemic activity in alloxan-induced diabetic mice. THDP-3 can promote glycogen synthesis and inhibit gluconeogenesis to reduce blood glucose, which was related to the key hepatic glycogen metabolism related enzymes including glucokinase (GK), phosphoenolpyruvate carboxykinase (PEPCK), glucose-6-phosphatase (G6Pase) and AMP-activated protein kinase (AMPK) (Ru et al., 2019). THP, a water-soluble polysaccharide from *T. hemsleyanum* showed significantly hypoglycemic activities on alloxan-induced mice. The result of histopathological staining compared with glibenclamide in alloxan-induced mice indicate that it could restore the structure of pancreas, and had low side effects on the liver or kidney. Thus, this study provided a mechanistic basis that THP (**89**) could be used as a potential natural candidate for diabetes with little side effect (Ru et al., 2018). Tetrastigmindole A (**153**), *cis*-apigenin-6-vinyl-7″-rhamnoside (**37**) and apigenin-8-*C*-[6-deoxy-2-*O*-(α-*L*-rhamnopyranosyl)-*xylo*-hexopyranos-3-uloside (**6**) from *T. obtectum* showed potential anti-diabetic effects by enhancing the GLUT4 translocation and promoting absorption of glucose (Shi, 2012).

### 4.6. Antiviral bioactivity

The antiviral bioactivity of rutin (**62**), kaempferol (**45**), astragalin (**39**), quercitrin (**56**), quercetin (**55**), kaempferol-3-*O*-rutinoside (**50**), procyanidin dimmer (**71**) and epicatechin (**65**) from the dried rhizome parts of *T. hemsleyanum* was explored by correlation analysis statistical method. The result indicated that those compounds were positively related to antiviral activity (Ding et al., 2019). The *n*-butanol and ethyl acetate extracts of *T. hemsleyanum* exhibited antiviral bioactivity against RSV (respiratory syncytial virus) with therapeutic index (T1) values of **128** and **64**, respectively. They were obviously superior to ribavirin (T1 = 6.25) (Wang et al., 2019). The extracts of *T. hemsleyanum* (petroleum ether, ethyl acetate, dichloromethane and n-butanol extracts) had inhibitory effects on hepatitis B virus (HBV) by decreasing the secretion of HbsAg and HbeAg (Yang & Wu, 2009). *T. hemsleyanum* leaves extract (THLE) exhibited protective effects against acrylamide-induced toxicity in HepG2 cells and *Caenorhabditis elegans* by *in vivo* and *in vitro* models and 5-caffeoylquinic acid was the key active component. DAF-16/FOXO gene was involved in the protective effect via regulating the expression levels of downstream antioxidant genes (Chu et al., 2020). The alcohol extract from root tuber of *T. hemsleyanum* could improve the survival rate of mice infected with influenza A H1N1 virus by reducing the damage of exgenous viruses to cell, enhancing spleen T cell proliferation and NK cell killing activity, improving the cellular immune function of mice. Its mechanism of action may be related to the up-regulation of the concentration of pro-inflammatory factor IFN-γ and IL-2 in serum and lung tissue, downregulating the concentration of inflammatory factor INF-α in serum or inhibiting the up-regulation of the concentration of inflammatory factor TNF-α in lung tissue (Liu, 2019).

### 4.7. Other activities

The flavonoids of *T. hemsleyanum* indicated remarkable inhibitory on viability and proliferation of leukemia NB-4 cells using CCk8 assay and BrdU test, the $IC_{50}$ at 48 h was 2.26 g/L. Furthermore, it could induce apoptosis of leukemia NB-4 cells through the p38 MAPK signal pathway and the pathway of apoptotic proteins (Wu et al., 2019). *T. hypoglaucum* had a protective effect on myocardial ischemia reperfusion injury. It could reduce myocardial cells injury, and alleviate oxidative stress and inflammatory reaction (Wang et al., 2017). The extract of *T. hemsleyanum* could promote the proliferation and function changes of NK cells in patients with chronic hepatitis B, and up-regulate the NK cell surface expression of PFP, GrB, CD107a and IFN-γ (Wang et al., 2018). *T. hypoglaucum* extract displayed a strong bacteriostasis effect testing with the bacteriostasis of TCM. Its MICs (minimal inhibitory concentrations) against 55 strains of MRSE (methicillin-resistant *Staphylococcus epidermidis*) and 43 strains of MSSE (methicillin-resistant and sensitive *S. epidermidis*) were 1185 μg/mL and 286 μg/mL ($p < 0.05$), respectively (Wang et al., 2016). The monomeric compounds are summarized in Table 3, and the extracts are summarized in Table 4.

## 5. Progress in clinical applications

### 5.1. Treatment of malignant tumor-related diseases

In the clinical application, Sanyeqing (*T. hemsleyanum*) was mainly used for treatment of malignant tumor. The tiple-negative breast cancer (TNBC) patient took *Sanyeqing Sanjie Kang'ai Formula* (containing herbal medicine Sanyeqing), and the result showed the treatment group's pathological complete response (pCR rate) was 30.43% and 31.25% (Lv et al., 2014). Wei (2007) used

**Table 3**
Compound sources and pharmacological effects.

| Compound names | Plant sources | Activities | Models/Methods | Results | References |
|---|---|---|---|---|---|
| Apigenin **1** | *T. hemsleyanum* | Antitumor activity | HepG2, HCT-8 and A549 tumor cells | $IC_{50}$ values of (73.16 ± 0.96), (45.04 ± 1.25) and (48.66 ± 1.56) μg/mL, respectively | Lin et al. (2015) |
| Astragalin **39** | *T. hemsleyanum* | Antitumor activity | HePG2 | $IC_{50}$ values of (592 ± 3.31) μg/mL | Sun et al. (2015) |
| Catechin **65** | *T. hemsleyanum* | Antitumor activity | HePG2 | $IC_{50}$ values of (218.31 ± 2.38) μg/mL | Sun et al. (2015) |
| Isoquercitrin **41** | *T. hemsleyanum* | Antitumor activity | NBT-II cells | Blocking the migration of NBT-II cells and inhibiting HGF/SF-mediated cell motility and invasion *in vitro*, inhibiting metastasis of HGF autocrine NBT-II cells *in vivo* | Xia et al. (2018) |
| Kaempferol **45** | *T. hemsleyanum* | Antitumor activity | MDA-MB-435 s cell investigated by MTT | $IC_{50}$ values of 294.3 μg/mL | Chen (2014) |
| Kaempferol-3-rutinoside **50** | *T. hemsleyanum* | Antitumor activity | HePG2 | $IC_{50}$ values of (389.71 ± 4.23) μg/mL | Sun et al. (2015) |
| Oleanolic acid **94** | *T. hemsleyanum* | Antitumor activity | Hela229 cell and A375 cell | Cytotoxic activities against Hela229 and A375 cell with $IC_{50}$ values of 25.69 μg/mL and 69.87 μg/mL | Ding et al. (2015) |
| Rutin **62** | *T. hemsleyanum* | Antitumor activity | HePG2 | $IC_{50}$ values of (312.23 ± 1.17) μg/mL | Sun et al. (2015) |
| Resveratrol **196** | *T. hemsleyanum* | Antitumor activity | MDA-MB-435 s cell investigated by MTT | $IC_{50}$ values of 92.4 μg/mL | Chen (2014) |
| RTP-3-1 **86** | *T. hemsleyanum* | Antitumor activity | SGC-7901 cell | Inducing apoptosis of SGC-7901 cell in a dose-dependent manner | Guo (2018) |
| *β*-Sitosterol **106** | *T. hemsleyanum* | Antitumor activity | Hela229 cell | Cytotoxic activities against Hela229 with $IC_{50}$ values of 40.78 μg/mL | Ding et al. (2015) |
| *p*-Hydroxybenzoic acid **206** | *T. hemsleyanum* | Antitumor activity | MDA-MB-435 cell | $IC_{50}$ values of (92.39 ± 1.68) μg/mL | Lin et al. (2016) |
| Astragalin **39** | *T. hemsleyanum* | Antiviral activity | Correlation analysis statistical method with SPSS software between LC-MS chemometrics and bioactivity of infuenza virus inhibition | Antiviral activity with the correlation coefficient of 0.711 | Ding et al. (2019) |
| Epicatechin **63** | *T. hemsleyanum* | Antiviral activity | Correlation analysis statistical method with SPSS software between LC-MS chemometrics and bioactivity of infuenza virus inhibition | Antiviral activity with the correlation coefficient of 0.641 | Ding et al. (2019) |
| Kaempferol **45** | *T. hemsleyanum* | Antiviral activity | Correlation analysis statistical method with SPSS software between LC-MS chemometrics and bioactivity of infuenza virus inhibition | Antiviral activity with the correlation coefficient of 0.580 | Ding et al. (2019) |
| Kaempferol-3-*O*-rutinoside **50** | *T. hemsleyanum* | Antiviral activity | Correlation analysis statistical method with SPSS software between LC-MS chemometrics and bioactivity of infuenza virus inhibition | Antiviral activity with the correlation coefficient of 0.514 | Ding et al. (2019) |
| Procyanidin dimmer **71** | *T. hemsleyanum* | Antiviral activity | Correlation analysis statistical method with SPSS software between LC-MS chemometrics and bioactivity of infuenza virus inhibition | Antiviral activity with the correlation coefficient of 0.503 | Ding et al. (2019) |
| Quercitrin **56** | *T. hemsleyanum* | Antiviral activity | Correlation analysis statistical method with SPSS software between LC-MS chemometrics and bioactivity of infuenza virus inhibition | Antiviral activity with the correlation coefficient of 0.617 | Ding et al. (2019) |
| Quercetin **55** | *T. hemsleyanum* | Antiviral activity | Correlation analysis statistical method with SPSS software between LC-MS chemometrics and bioactivity of infuenza virus inhibition | Antiviral activity with the correlation coefficient of 0.614 | Ding et al. (2019) |
| Rutin **62** | *T. hemsleyanum* | Antiviral activity | Correlation analysis statistical method with SPSS sofware between LC-MS chemometrics and bioactivity of infuenza virus inhibition | Antiviral activity with the correlation coefficient of 0.547 | Ding et al. (2019) |
| Apigenin-6-*C*-*α*-*L*-rhmnnopyranosyl-(1-4)-*α*- | *T. hemsleyanum* | Enhancing Immune activity | Lymphocyte proliferation assay investigated by MTT and hemolysis plaque formation assay | Enhancing the ConA -induced T cell proliferation response and increasing the production of antibody forming cells in mice | Liu (2000) |

Table 3 (*continued*)

| Compound names | Plant sources | Activities | Models/Methods | Results | References |
|---|---|---|---|---|---|
| *L*-Arabinopymnoside **89** | | | | | |
| Apigenin-6,8-di-*C*-*β*-*D*-glucopyranoside **4** | *T. hemsleyanum* | Enhancing immune activity | Lymphocyte proliferation assay investigated by MTT and hemolysis plaque formation assay | Enhancing the ConA-induced T cell proliferation response and increasing the production of antibody forming cells in mice | Liu (2000) |
| Catechin **65** | *T. hypoglaucum* | Enhancing immune activity | Lymphocyte proliferation assay investigated by MTT and hemolysis plaque formation assay | Enhancing the ConA-induced T cell proliferation response and increasing the production of antibody forming cells in mice | Liu (2000) |
| 6-Hydroxy-3,4-dihydro-1-oxo-*β*-carboline **151** | *T. hemsleyanum* | Anti-inflammatory activity | Measuring NO production in LPS-induced RAW264.7 macrophages | $IC_{50}$ values of 31.9 μmol/L | Wang et al. (2018) |
| Hippophamide **152** | *T. hemsleyanum* | Anti-inflammatory activity | Measuring NO production in LPS-induced RAW264.7 macrophages | $IC_{50}$ values of 25.2 μmol/L | Wang et al. (2018) |
| *S*-(-)-Trolline **155** | *T. hemsleyanum* | Anti-inflammatory activity | Measuring NO production in LPS-induced RAW264.7 macrophages | $IC_{50}$ values of 6.3 μmol/L | Wang et al. (2018) |
| Apigenin-8-*C*-[6-deoxy-2-*O*-(*α*-*L*-rhamnopyranosyl) -*xylo*-hexopyranos-3-uloside] **6** | *T. obtectum* | Anti-diabetic activity | The experiment of GLUT4 translocation in skeletal muscle L6 cells | Enhancing the GLUT4 translocation and promoting the absorption of glucose | Shi (2012) |
| *cis*-Apigenin-6-vinyl-7″-Rhamnoside **37** | *T. obtectum* | Anti-diabetic activity | The experimem of GLUT4 translocation in skeletal muscle L6 cells | Enhancing the GLUT4 translocation and promoting the absorption of glucose | Shi (2012) |
| Tetrastigmindole A **153** | *T. obtectum* | Anti-diabetic activity | The experimem of GLUT4 translocation in skeletal muscle L6 cells | Enhancing the GLUT4 translocation and promoting the absorption of glucose | Shi (2012) |
| Tetrastigmindole A **153** | *T. obtectum* | Antitumor activity | MD-MBA-231cell lines *in vitro* | Inhibition rates at a concentration of 20 μg/mL, 1 μg/mL, 0.05 μg/mL were 70.3%, 34.4% and 28.2%, respectively | Shi (2012) |
| Tetrastigmindole B **154** | *T. obtectum* | Antitumor activity | MD-MBA-231cell lines investigated by transwell chemotaxis method | Inhibition rates at a concentration of 20 μg/mL, 1 μg/mL, 0.05 μg/mL were 59.2%, 40.8% and 11.1%, respectively | Shi (2012) |
| 3*β*-Hydroxystigmast-5-en-7-one **114** | *T. planicaule* | Antitumor activity | CNE cells investigated by MTT | Cytotoxic activities against CNE cell with $IC_{50}$ of 44.2 μg/mL | Shao (2011) |
| 7*α*-Hydroxysitosterol **110** | *T. planicaule* | Antitumor activity | CNE cells investigated by MTT | Cytotoxic activities against CNE cell with $IC_{50}$ of 65.63 μg/mL | Shao (2011) |
| Protocatechuic acid **205** | *T. planicaule* | Antitumor activity | CNE cells investigated by MTT | Cytotoxic activities against CNE cell with $IC_{50}$ of 76.75 μg/mL | Shao (2011) |
| SYQP **91** | *T. hemsleyanum* | Antipyretic and antitumor activities | Brewer's yeast induced hyperthermia test and H22 tumor bearing mice | Reducing the hyperthermia temperature of the mice induced by Brew's yeast and decreasing PGE2, markedly suppressing the inhibiting the growth of H22 tumor in mice with inhibitory rate of 39.9% | Zhu et al. (2020) |
| TDGP-3 **88** | *T. hemsleyanum* | Antioxidant and antihyperlipidemic activities | HFD-induced hyperlipidemia mice | Repressing the weight gain induced by HFD, obviously reversing the increased TC, TG, and LDL-C level and the decreased HDL-C level in mice with HFD. increasing the levels of SOD, CAT and GSH-Px ($p < 0.01$) and obviously decreasing the accumulation of MDA ($p < 0.01$) | Ru et al. (2019 a) |
| THDP-3 **87** | *T. hemsleyanum* | Hypoglycemic activity | Alloxan-induced diabetic mice | Significantly reducing blood glucose levels in alloxan-induced diabetic mice ($p < 0.01$) and decreasing content of hepatic glycogen ($p < 0.01$) | Ru et al. (2019b) |
| THP **98** | *T. hemsleyanum* | Hypoglycemic effects | Alloxan-induced diabetic mice | Decreasing the blood glucose, TC, TG, LDL-C levels and increasing the body weight, HDL-C and insulin levels of mice, enhancing the activities of antioxidant enzyme system in mice | Ru et al. (2018) |
| Catechin **63** | *T. erubescens* | Antioxidant activity | DPPH assay and lipid peroxidation inhibition assays *in vitro* | $IC_{50}$ of 5.4 μmol/L and 379.2 μmol/L, respectively | Dao et al. (2014) |
| Epicatechin-3-*O*-gallate **65** | *T. erubescens* | Antioxidant activity | DPPH assay and lipid peroxidation inhibition assays *in vitro* | $IC_{50}$ of 2.2 μ mol/L and 52.1 μmol/L, respectively | Dao et al. (2014) |
| (*E*)-Resveratrol **196** | *T. erubescens* | Antioxidant activity | DPPH assay and lipid peroxidation inhibition assays *in vitro* | $IC_{50}$ of 31.3 μ mol/L and 607.5 μmol/L, respectively | Dao et al. (2014) |
| (*E*) 2,3,5,4′-Tetrahydroxystilbene-2-*O*-β-*D*-glucoside **199** | *T. erubescens* | Antioxidant activity | DPPH assay and lipid peroxidation inhibition assays *in vitro* | $IC_{50}$ of 31.1 μmol/L and 157.3 μmol/L, respectively | Dao et al. (2014) |
| (+)-Lyoniresinol **145** | *T. erubescens* | Antioxidant activity | DPPH assay *in vitro* | $IC_{50}$ of 8.8 μmol/L | Dao et al. (2014) |

(*continued on next page*)

**Table 3** (*continued*)

| Compound names | Plant sources | Activities | Models/Methods | Results | References |
|---|---|---|---|---|---|
| Phlorizin **68** | *T. erubescens* | Antioxidant activity | DPPH assay and lipid peroxidation inhibition assays *in vitro* | $IC_{50}$ of 60.4 μmol/L and 364.7 μmol/L, respectively | Dao et al. (2014) |
| Tetrastigmol A **217** | *T. erubescens* | Antioxidant activity | DPPH assay and lipid peroxidation inhibition assays *in vitro* | $IC_{50}$ of 9.5 μmol/L and 87.8 μmol/L, respectively | Dao et al. (2014) |
| 3-*O*-Galloybergenin **129** | *T. erubescens* | Antioxidant activity | DPPH assay and lipid peroxidation inhibition assays *in vitro* | $IC_{50}$ of 1.8 μmol/L and 60.9 μmol/L, respectively | Dao et al. (2014) |

Note: CAT, catalase from micrococcus lysodeikticus; DPPH, the stable free radical; EMT, epithelial mesenchymal transition; GLUT4, glucose transporters 4; GSH-Px, gluthathione peroxidase; HFD, high-fat diet; HGF/SF, hepatocyte growth factor/scatter factor; HDL-C, low levels of high density lipoprotein; LPS, lipopolysaccharide; LDL-C, low density lipoprotein; MDA, Malondialdehyde; Met, is involved in the development and progression of many human cancers; NO, nitric oxide; PGE2, prostaglandin E2; SOD, superoxide Dismutase; TC, total cholesterol; TG, triglycerides.

praeparatum-Jinqi Pian (Taking herbal medicine Sanyeqing as the main ingredient with *Astragal Radix* and ginsenoside) to treat 120 cases of patients with malignant tumor. The results indicated 52 patients were recovered and the overall efficiency was 78.33%. In addition, praeparatum Jinqi Pian (Taking herbal medicine Sanyeqing as the main ingredient with *Astragal Radix* and ginsenoside) was suitable for long-term health food for cancer patients and people with low immunity. Jiang and Gong (2005) used Zhonggan Oral Liquid (containing Sanyeqing) to treat 112 cases of patients with primary carcinoma of liver. The result showed treatment group's survival rate was 43.1%. Shi (Xu et al., 2015) created a prescription named Zhengyuan Yiliu Fang (containing Sanyeqing) to treat malignant lymphoma, which obtains great efficacy in clinical studies.

### 5.2. Treatment of other diseases

Li (2001) developed an innovative Chinese medicine (using Sanyeqing and other materials) for the treatment of chronic hepatitis B pneumonia. Many studies showed this medicine had the functions of inhibiting hepatitis B virus, regulating body's immunity. Xu (2006) established a prescription named Sanyeqing Shigao Tang (taking Sanyeqing as the main ingredient with raw gypsum) to treat 72 cases of exogenous fever in children.The result indicated 22 patients were recovered with the total efficiency of 94.4%. Ji (2020) found that Sanyeqing had a good effect on the treatment of redness, swelling, inflammation, ulceration and other symptoms after mosquito bited. Zhou (2013) used Hugan Toudu decoction containing 20 g of Sanyeqing to treat 228 cases of chronic hepatitis B. The result showed that the total efficiency of the Hugan Toudu decoction group was higher than the Chinese patent medicine group and modern medicines group ($p < 0.01$). In some areas of China, Sanyeqing was also used for the treatment of common gynecological diseases such as hemorrhage, leucorrhea, measles complicated with pneumonia, anal fissure, chronic bronchitis, etc, and had good therapeutic effect on high fever and low fever cough in clinical (Liu & Wei, 2018). Ge (2012) established an oral liquid with dozens of herbal medicines such as Biandanteng (*T. planicaule*), combined with the Zhuang ethnomedicine Taiji-acupuncture and moxibustion to treat 113 cases of patient with chronic lumbar muscle strain. The result indicated 76 cases were cured and the total efficiency was 92.03%. Lu (2001) formulated a prescription named *Qigui Qianjinba Tang* with over ten herbal medicines including Biandanteng to treat 80 cases of patient with arthralgia syndrome. The treatment results showed 14 patients (17.5%) were cured and the total efficiency was 90%. Zhang et al. (2016) developed an external uses of Chinese medicine prescription (taking herbal medicine *T. planicaule* as the main ingredient) for treatment of rheumatism. This prescription displayed a high clinical improvement effect on rheumatism related diseases such as rheumatoid arthritis. Chen (Chen, 2000) used the juice from the rattan of *T. planicaule* to treat 37 cases of bovine with traumatic keratitis. The result indicated that 33 cases were cured, and the total efficiency 89.2%. This result also showed *T. planicaule* could improve micro blood circulation, dissipate inflammation and blood stasis, remove nebula for improving eyesight. Two cases of patient with coronavirus disease 2019 (COVID-19) were treated with some prescriptions (containing Sanyeqing and other Chinese medicines) for therapy of integrating traditional Chinese medicine and Western medicine. The clinical studies showed one case of was cured and another one was remarkably relieved with outing of critical condition (He et al., 2020). Yu (Sun et al., 2021) treated one case of children with recurrent suppurative tonsillitis with some prescriptions (containing Sanyeqing and other Chinese medicines). The result indicated the children was cured after four times treatment with little recurrence within half a year. Sanyeqing had the

**Table 4**
Sources of plant parts and pharmacological effects.

| Extracts | Activities | Models/Methods | Results | References |
|---|---|---|---|---|
| Ethylacetate extracts of *T. hemsleyanum* | Antitumor activity | Nude mice bearing colorectal cancer with HT29 cells | Inhibiting the growth of HT29 cells subcutaneously transplanted tumor and its inhibitory rate of low, medium and high dose treatment groups were 8.13%, 21.75%, 37.8%, respectively | Lin et al. (2016) |
| Ethylacetate extracts of *T. hemsleyanum* | Antitumor activity | Mice inoculated with HepG-2 cell | Inhibiting athymic mouse transplantation tumor and its inhibitory rate of low, medium and high dose treatment groups were 38. 66%, 23.53% and 31.09%, respectively | Wang et al. (2014) |
| Ethylacetate extracts of *T. hemsleyanum* | Antitumor activity | HCCC-9810 cells | $IC_{50}$ of ETH treatment for 24 h, 48 h and 72 h were 275.3 mg/L, 183.3 mg/L and 75.8 mg/L, respectively | Wang et al. (2015) |
| Ethylacetate extracts of *T. hemsleyanum* | Anti-HBV activity | HepG2.2.15 cells | Significantly restraining the secretion of HBsAg and HbeAg from HepG2.2.15 cells | Yang et al. (2009) |
| Ethylacetate fraction of extracts from *T. hemsleyanum* | The immune-regulatory | ICR mice | Increasing the mouse spleen lymphocyte transformation induced by ConA, the left-hind voix pedis thickness and the number of PFCs, increasing the ink clearance ability, increasing the phagocytosis index of mononuclear-macrophages and production of IFN-γ, promoting the production of IFN-α | Xu et al. (2008) |
| Water, ethanol and ethyl acetate extracts of *T. hemsleyanum* | Antitumor activity | MCF-7 cells *in vitro* | Inhibiting MCF-7 cells in a dose-dependent manner ($p < 0.05$) and promoting the apoptosis of MCF-7 cells ($p < 0.05$) | Qiu et al. (2018) |
| Water extract from tuber of *T. hemsleyanum* | Antitumor activity | BGC-823 cells and NK cells *in vitro* | Promoting the proliferation of NK cells and enhancing the cytotoxic activity of NK cells to BGC-823 cells with the maximum (67.75 ± 2.58) % | Yuan et al. (2016) |
| Water extract from tuber of *T. hemsleyanum* | Antitumor activity | MDA-MB-435 cells investigated by MTT *in vitro* | $IC_{50}$ values of 127.8 μg/mL | Chen (2014) |
| Water extract of *T. hemsleyanum* | Anti-inflammatory activity | COPD copied by being smoked and LPS in rat | The contents of TNF-α and IL-1β, the total number of white blood cells and neutrophils were significantly decreased | Jiang et al. (2018) |
| Water extract of whole plant of *T. hypogtaucum* | Anti-inflammatory activity | The myocardial ischemia reperfusion injury in rats. | Reducing myocardial cells injury, alleviating oxidative stress and inflammatory reaction | Wang et al. (2017) |
| Water extract of *T. hemsleyanum* | Anti-inflammatory activity | COPD copied by being smoked and LPS in rat | MMP-9 and TIMP-1 content decreased significantly ($p < 0.05$) | Jiang et al. (2016) |
| Water extract of *T. hypoglaucum* | Antibacterial activity | Methicillin-resistant *Staphylococcus epidermidis* and methicillin-resistant and sensitive *S. epidermidis* | Stronger bacteriostasis effect with the MIC of 1185 μg/mL and 286 μg/mL, respectively | Wang et al. (2016) |
| Ethanol extract of *T. obtectum* | Anti-inflammatory and analgesic activity | The xylene ear swelling model and the acetic acid writhing experiment in mouse | Inhibitory effect on ear swelling caused by xylene and writhing caused by acetic acid in mice | Li et al. (2018 a) |
| Ethanol extract of *T. hemsleyanum* | Hepatoprotective activity | ANIT-induced liver injury in mice | The levels of TBIL and TNF-α were significantly decreased ($p < 0.05$), the levels of ALT, AST, TBA, TBIL and TNF-α in serum were decreased, and the MDA content were significantly decreased | Li et al. (2018b) |
| Ethanol extract of *T. planicaule* | Hepatoprotective activity | $CCl_4$-induced acute liver injury in mice | Significantly resisting the increase of ALT and AST, downregulating MDA content of liver homogenate, and improving SOD activity | Bin et al. (2016) |
| Ethanol extract *T. hemsleyanum* | Antiviral activity | HepG2 cells | The protective effect against ACR-induced toxicity in HepG2 cells and attenuating ACR-induced toxicity in HepG2 cell via regulating Akt/mTOR/FOXO1/MAPK signaling pathway | Chu et al. (2020) |
| Petroleum ether, *n*-butanol fraction of *T. planicaule* | Antitumor activity | HepG-2 cells investigated by MTT | Obvious antitumor activity against the growth of HepG-2 cells | Chen (2017) |
| Petroleum ether fraction, ethylacetate fraction, *n*-butanol fraction and water fraction from *T. planicaule* | Antioxidant activity | FRAP assay, OH· scavenging assay, and ABTS$^{+}$ ·scavenging assay | Ferric reducing antioxidant of them were weaker than VC, but higher than tea polyphenol except water fraction | Pan et al. (2013) |
| Methanol extract of the aerial parts of *T. hemsleyanum* | Anti-inflammatory activity | RAW264.7 cells | Considerable inhibitory effect on LPS-stimulated NO production in RAW264.7 macrophages ($IC_{50}$: 22.69 ± 0.75 μmol/L) | Wang et al. (2018a) |
| *n*-Butanol extract and ethyl acetate extract of the ethanol extract of *T. hemsleyanum* | Antiviral activity | MA104 cell | The TI of *n*-butanol and ethyl acetate extraction were 128 and 64, respectively | Wang et al. (2019) |
| Polysaccharides from the aerial parts of *T. hemsleyanum* | Antitumor activity | Mice inoculated with 4 T1 cell | Effectively inhibiting tumor growth and distal lung metastasis | Guo et al. (2019) |
| Flavonoid fraction extracted from *T. hemsleyanum* | Antitumor activity | Spleen mononuclear cells of mice with lung cancer | PGE2 and COX-2 were significantly reduced ($p < 0.01$) | Zhang et al. (2019b) |
| Flavonoid fraction extracted from *T. hemsleyanum* | Antitumor activity | A549 cells investigated by miRNA-seq and bioinformatics technology | Intracellular endocytosis pathway was significantly enriched | Wei et al. (2018) |
| Flavonoid fraction extracted | Antitumor | A549 cells investigated by MTT, | Inhibiting the proliferation of lung cancer A549 cells in a | Zhong |

(*continued on next page*)

**Table 4** (*continued*)

| Extracts | Activities | Models/Methods | Results | References |
|---|---|---|---|---|
| from *T. hemsleyanum* | activity | enzyme proteasome assay, Real-time PCR and Western blot *in vitro* | dose-dependent manner ($p$ < 0.05), reducing the activity of proteasome and DUB, up-regulating the protein expression of ub-prs and down-regulating the protein expression of USP14, UCHL5, POH1 | et al. (2017) |
| Flavonoid fraction extracted from *T. hemsleyanum* | Antitumor activity | LPS induced ALI of aged C57BL/6J mice | Significantly reducing leukocyte, especially neutrophil infiltration in BALF, inhibiting IL-1β, IL-6, IL-12p40, TNF-α and s TNF-R1 secretion ($p$ < 0.01), improving pathohistological change of lung tissues, significantly attenuating the phosphorylation of p38 MAPK, NF-κB and the activity of NF-κB ($p$ < 0.01) | Liu et al. (2015) |
| Flavonoid fraction extracted from *T. hemsleyanum* | Antitumor activity | NB-4 cells investigated by CCK-8 assay, BrdU test and Flow cytometry | 1. Inhibiting the viability and proliferation of NB-4 cells in a time- and dose-dependent manner, and the $IC_{50}$ at 48 h was 2.26 g/L<br>2. Inducing apoptosis of the NB-4 cells, down-regulating the expression of anti-apoptotic protein Bcl-2, and up-regulating the expression of pro-apoptotic proteins Bax, caspase-3 and Cyt-C in a dose-dependent manner ($p$ < 0.05), decreasing the expression of ERK5 and increasing the expression of p38 | Wu et al. (2019) |
| Flavonoid fraction extracted from *T. hemsleyanum* | Antitumor activity | C57BL/6 mice inoculated with LLC cells | Significantly inhibiting tumor growth and suppressing regulatory T-cell development | Feng et al. (2014) |
| Flavonoid fraction extracted from *T. planicaule* | Antioxidant activity | FRAP assay, salicylic acid assay and ABTS assay | The activity of reducing $Fe^{3+}$ antioxidant and scavenging ABTS + ·was higher than tea polyphenol, but scavenging OH· was lower than VC and tea polyphenol | Pan et al. (2012) |

Note: ACR, acrylamide; ANIT, α-isothiocyanatoacetate; ALI, acute lung injury; ALT, alanine aminotransferase; AST, aspartate aminotransferase; BALF, bronchoalveolar lavage fluid; COPD, chronic obstructive pulmonary disease; COX-2, cyclooxygenase-2; DUB, deubiquitinating enzyme; ERK5, extracellular signal-regulated kinase 5; HBeAg, hepatitis Be antigen; HBeAg, hepatitis Be antigen; IL-1β, interleukin-1β; IL-1β, interleukin-1β; IL-6, interleukin- 6, IL-12p40, interleukin-12p40; IFN-γ, serum interferon-gamma; IFN-α, serum tumor necrosis factor-alpha; LPS, lipopolysaccharide; PGE2, prostaglandin 2; MDA, malondialdehyde; MAPK, mitogen-activated protein kinase; MMP-9, matrix met alloproteinases-9; NF-κB, nuclear factor kappa-B; TIMP-1, matrix met alloproteinases inhibitor-1; PFCs, plague forming cells; SOD, superoxide dismutase; TBIL, total bilirubin; TNF-α, tumor necrosis factor-α, TNF-R1, tumor necrosis factor receptor 1,TBA, total bile acid; USP14, ubiquitin-specific proteases 14; UCHL5, recombinant ubiquitin carboxyl terminal hydrolase L5; VC, Vitamin C.

functions of clearing away heat and detoxification, promoting blood circulation, dispersing masses, reducing inflammation and pain, dispelling wind and phlegm, regulating qi and strengthening spleen, *etc*. Based on clinical experience, it was believed to have played a key role in the treatment of children with recurrent suppurative tonsillitis.

## 6. Conclusion and outlook

The *Tetrastigma* species had many interesting chemical constituents and obvious pharmacological activities. Therefore, *Tetrastigma* species could be considered a potential candidate of nutritional supplement and new drug discovery. This review summarized 248 secondary metabolites of species in genus *Tetrastigma* including flavonoids, saccharides, terpenoids, steroids, phenylpropanoids and alkaloids, described the recent advance in pharmacological activities of the extracts and the metabolites from *Tetrastigma* species, and summarized the folk uses and up-to date clinical treatments of *Tetrastigma* species. Plants of *Tetrastigma species* were most commonly used in the treatment of tumor-related diseases and had definite curative effect, and the extracts and compounds of *Tetrastigma* species exhibited obvious antitumor activity. It provided preliminary evidence of the relationship between modern pharmacological studies and folk uses of anti-tumor. The underlying mechanism may be related to inhibiting tumor cell proliferation, inducing cell apoptosis, inhibiting tumor cell migration and invasion, inhibiting tumor cell angiogenesis, reversing tumor cell multidrug resistance, regulating the body's own immunity and so on. Furthermore, the folk uses of these species are the treatment of pneumonia, nephritis, hepatitis, rheumatism, arthralgia, traumatic, injury, inflammation, fever, snakebites, etc. Pharmacological properties such as antiviral, anti-inflammatory and analgesic activities have supported the traditional uses of *Tetrastigma* species. It was noteworthy that the anti-diabetic effect was a new biological activity discovered in recent years.

However, there are still yet some problems in the further development of *Tetrastigma* species. Firstly, to date most studies focused mainly on the *T. hemsleyanum*, while the phytochemical and biological activities and clinical researches of the other species were not comprehensively investigated. In order to expand and develop new medicinal sources, more studies should be done on other species. What's more, the resources of *T. hemsleyanum* are limited, which greatly restrict their utilization and development. Therefore, a well-developed cultivation technique will be needed to establish. Secondly, existing pharmacological and biological activity researches were insufficient to clarify the relationship between traditional functions and clinical applications and the mechanism of action. As such, it is necessary to deepen the research on the pharmacological mechanism and analyses of the structure–activity relationships of secondary metabolites of *Tetrastigma* species in the future. Finally, the quality control of *Tetrastigma* species is poorly investigated. Thus, the well-developed analytical methods are needed to ensure their consistency, safety and efficacy. This article could be a useful tool in assisting researchers to discoveri new drug candidates for further research and provides an incentive to expand the research of genus *Tetrastigma.*

## Editor Note

Wei Wang is Editorial Board Members of Chinese Herbal Medicines. He was blinded from reviewing or making decisions on the manuscript. The article was subject to the journal's standard procedures, with peer review handled independently of this Editorial Board Member and their research groups.

## Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

## Acknowledgements

We thank for the funding support from the National Natural Science Foundation of China, China (No. 81703819 and No. 81874369), Hunan Key Laboratory of Druggability and Preparation Modification for Traditional Chinese Medicine (No. 2017-04), Hunan Provincial Key Laboratory of Dong Medicine (No. 2015TP1020-02) and Students Research Innovative Program of Hunan Province (No. 2018-413).

## References

Bin, X., Pan, Q. D., Huang, Y. H., Han, J. D., Wu, L. Q., Nong, J. Y., et al. (2016). Protective effects of alcohol extract from *Tetrastigma planicaule* (Hook.f.) Gagnep on acute liver injury induced by $CCl_4$ in mice. *Journal of Youjiang Medical College for Nationalities, 38*(1), 17–19.
Cai, W. W., Chen, D., & Fan, S. M. (2014). Research review on chemical components and pharmacological effects of *Tetrastigmatis hemsleyanum*. *Tianjin Pharmacy, 26* (1), 38–41.
Cai, Y. W., Ji, S. L., Xiang, D. S., Hong, X. L., Sang, K. L., Wang, H. S., et al. (2018). Three new constituents from the aerial parts of *Tetrastigma hemsleyanum*. *Phytochemistry Letters, 27*, 25–29.
Chen, H. L. (2000). Treatment of bovine traumatic keratitis with *Tetrastigma planicaule* (Hook.f,) Gagnep. Fujian Animal Husbandry Veterinary, (02), 34.
Chen, L. Y. (2014). *Study on the chemical constituents and the antitumor activity of Tetrastigma hemsleyani*. Fujian University of Traditional Chinese Medicine. PhD Thesis of Master Degree.
Chen, S. B. (2017). *Studies on the constituents from Yao medicine Tetrastigma planicaul*. Guangxi University of Traditional Chinese Medicine. PhD Thesis of Master Degree.
Cheng, Q., & Fu, H. (2016). Study development on pharmacological effect and clinical research of *Radix Tetrastigme*. *Journal of Liaoning University of Traditional Chinese Medicine, 18*(04), 235–238.
Chu, Q., Chen, W., Jia, R., Ye, X., Li, Y., Liu, Y., et al. (2020). *Tetrastigma hemsleyanum* leaves extract against acrylamide-induced toxicity in HepG2 cells and *Caenorhabditis elegans*. *Journal of Hazardous Materials, 393* 122364.
Chu, Q., Jia, R. Y., Chen, M., Li, Y. L., Yu, X., Wang, Y. X., et al. (2019). *Tetrastigma hemsleyanum* tubers polysaccharide ameliorates LPS-induced inflammation in macrophages and *Caenorhabditis elegans*. *International Journal of Biological Macromolecules, 141*, 611–621.
Dao, P. T. A., Quan, T. L., & Mai, N. T. T. (2014). Antioxidant constituents from the stem of *Tetrastigma erusbescense* Planch. (Vitaceae). *Natural Product Sciences, 20* (1), 22–28.
Ding, F., Liu, J., Du, R., Yu, Q., Gong, L., Jiang, H., et al. (2019). Qualitative and quantitative analysis for the chemical constituents of *Tetrastigma hemsleyanum* Diels et Gilg using ultra-high performance liquid chromatography/hybrid quadrupole-qrbitrap mass spectrometry and preliminary screening for anti-influenza virus components. *Journal of Evidence-Based Complementary & Alternative Medicine, 2019*(10), 12–70.
Ding, L., Zhang, L. X., Qiu, Y., & Wang, Y. H. (2015). Chemical constituents in chloroform extraction of *Tetrastigmatis hemsleyani* Diels et. Gilg and their antitumor activities. *Chinese Pharmaceutical Journal (Beijing, China), 50*(21), 1857–1860.
Du, C., Wang, Y., Zhang, Y. Y., Zhang, J. H., Zhang, L. F., & Li, J. R. (2020). Effects of total flavonoids of *Tetrastigma hemsleyanum* on proliferation and metastasis of breast cancer cells and its mechanism. *Acta Chinese Medicine, 35*(08), 1717–1722.
Fan, S. M., Xu, H. L., Xie, X. Y., Cai, B. Y., Zou, F. X., Xie, Z. S., et al. (2016). Study on UHPLC fingerprint and determination of eight phenolic components of *Tetrastigma hemsleyanum* leaves. *Chinese Journal of Traditional Chinese Medicine, 41*, 3975–3981.
Feng, Z. Q., Hao, W. R., Lin, X. Y., Fan, D. P., & Zhou, J. H. (2014). Antitumor activity of total flavonoids from *Tetrastigma hemsleyanum* Diels et Gilg is associated with the inhibition of regulatory T cells in mice. *Onco Targets and Therapy, 7*, 947–956.
Fu, Z. Q., Huang, Z. H., Lin, J., He, W. D., Ji, M. M., Xu, W., et al. (2015). Chemical constituents in root tuber of *Tetrastigma hemsleyanum* and their anti-oxidative activities. *Chinese Traditional and Herbal Drugs, 46*, 1583–1588.
Ge, C. L. (2012). Treatment of chronic lumbar muscle strain with zhuang medicine Tai Chi acupuncture moxibustion and Zhuang medicine. In *Proceedings of the Eighth External Academic Conference of the Chinese Academy of Traditional Chinese medicine* (pp. 379–438).
Guo, J. J., Zhao, Y. J., Li, W., Qian, C. D., & Ding, Z. S. (2019). Anti-tumor effects of polysaccharides from the aerial part of Sanyeqing on breast cancer mice. *Chinese Traditional Patent Medicine, 41*(004), 916–919.
Guo, N. S. (2018). *Extraction, purification, characterization and antitumor activity of polysaccharides from roots of Radix Tetrastigma*. Nanchang University. PhD Thesis of Master Degree.
Guo, X. J. (2013). *Chemical and bioactive studies of two species medicinal plants*. Shandong University. PhD Thesis of Master Degree.
He, Q., Ye, X. X., & Xu, B. (2020). Two cases of intergrative medicine treatment of new COVID-19. *Chinese Journal of Integrated Traditional and Western Medicine, 40* (03), 378–379.
Hu, T., Zhong, L. R., & Feng, Z. Q. (2021). Study on *Tetrastigma Hemsleyani Radix* flavones for MDSCs production and expression of related factors in mice with lung cancer. *Journal of New Chinese Medicine, 53*(08), 118–121.
Hu, Y., Cheng, L., Pu, J., Liang, W., & Zheng, J. (2013). GC-MS analysis of petroleum ether extract from *Tetrastigma hemsleyanum* Diels et. Gilg. *Chinese Journal of Traditional Medicine Science and Technology, 20*(01), 46–47.
Huang, H. W., Du, W. L., & Deng, Q. (2020). Effect of *Radix Tetrastigmae* extracts on proliferation of HeLa cells and its mechanism. *Zhejiang Medical Journal, 42*(06), 559–562.
Huang, Q., He, W., Khudoyberdiev, I., & Ye, C. L. (2021). Characterization of polysaccharides from *Tetrastigma hemsleyanum* Diels et Gilg Roots and their effects on antioxidant activity and $H_2O_2$-induced oxidative damage in RAW 264.7 cells. *BMC Chemistry, 15*(1), 9.
Huang, Y. Q. (2017). Microwave-assisted extraction process optimization of *Trifolium repens* polysaccharide and its antagonistic study on inflammatory cells. *Journal of Zhejiang University of Traditional Chinese Medicine, 52*(5), 384–385.
Huo, X., Yang, N., Liu, W., Gao, Y., & Liu, J. (2008). Determination of chemical constituents of the ether extract of *Radix Tetrastigmae hemsleyani*. *Chinese Journal of Pharmaceutical Analysis, 28*(10), 1651–1653.
Ji, Q. Y. (2020). Sanyeqing treats mosquito bites. *Journal of Traditional Chinese Medicine, 12*(10), 1–4.
Ji, T., Ji, W. W., Wang, J., Chen, H. J., Peng, X., Cheng, K. J., et al. (2021). A comprehensive review on traditional uses, chemical compositions, pharmacology properties and toxicology of *Tetrastigma hemsleyanum*. *Journal of Ethnopharmacology, 264* 113247.
Jiang, C. M., & Gong, L. Y. (2005). Treatment of 58 cases of primary liver cancer with zhonggan mixture. *Chinese Journal of Integrated Traditional and Western Medicine, 25*, 848–849.
Jiang, Y. J., Wang, X. L., Zhong, M., Xia, J. D., & Mo, Y. L. (2018). Effects of *Tetrastigma hemsleyani* water extract on tumor necrosis factor alpha and interleukin-1 betain chronic obstructive pulmonary disease. *Asia-Pacific Traditional Medicine, 14*(6), 13–15.
Jiang, Y. J., Wang, X. L., Zhong, M., Xia, J. D., Mo, Y. L., & Wang, Y. (2016). Influence of the water extract of *Radix Tetrastigma* on MMP-9 and TIMP-1 in rats of chronic obstructive pulmonary disease. *Strait Pharmaceutical Journal, 28*(06), 25–28.
Jin, P. F., Xu, S., Hui, H., Duan, H. Q., Zhao, C., & Tang, S. A. (2018). A new polyunsaturated lipid from *Tetrastigma hemsleyanum*. *Chemistry of Natural Compounds, 54*, 429–431.
Li, B., Liao, F. G., Huang, L. Y., & Chen, H. J. (2014). Chemical constituents of ethyl acetate fraction of *Tetrastigma planicaule*. *Journal of Chinese Medicinal Materials, 37*(04), 610–611.
Li, C. D. (2001). A new drug for the treatment of hepatitis B and its preparation method, CN1281701.
Li, J. (2020). *Chemical constituents of Phyllanthus acidus (L.) Skeel and Tetrastima planicaule*. Nanjing University Chinese Medicine. PhD Thesis of Master Degree.
Li, P., Ji, W. W., & Peng, X. (2018). Study on the the trifolium extract in anti ANIT-induced liver injury in mice. *China Modern Doctor, 56*(30), 38–41.
Li, Z. Y., Xiong, D. M., Lin, H. H., Zhou, Y. T., Liang, Z. C., & Wang, H. (2018). Study on the anti-inflammatory and analgesic effects of Miao medicine *Tetrastigma serrulatum* (Roxb.) Planch. *Journal of Qiannan Medical College for Nationalities, 31* (4). 243-244+270.
Lin, J., Ji, M. M., Huang, Z. H., Yu, H. M., Xu, W., & Fan, S. M. (2015). Chemical constituents of whole plants of *Tetrastigma hemsleyanum* and their antitumor activities. *Chinese Pharmaceutical Journal, 50*(8), 658–663.
Lin, S., Zhong, L. R., & Wei, K. M. (2016). Apoptosis-inducing effect of ethylacetate extracts of Sanyeqing (T*etrastigma hemsleyanum*) on colorectal cancer cell HT29 subcutaneous transplanted tumor. *Chinese Journal of Traditional Medical Science and Technology, 23*(5), 542–545.
Lin, Y. J., Chai, S. R., Long, K. L., Chen, J., Shi, J. M., & Xu, J. J. (2021). Effects of *Tetrastigma hemsleyanum* Diels et Gilg flavone on immune function and apoptosis-related proteins in tumor tissues of Lewis lung cancer mice. *Natural Product Research and Development, 33*(01), 8–15.
Lin, Z., Chen, L., Qi, Q., & Guo, S. (2016). Isolation and identification of antiproliferative compounds from the roots of *Tetrastigma hemsleyanum* against MDA-MB-435S cell lines. *Pakistan Journal of Pharmaceutical Sciences, 29*(4), 1171.
Liu, D. (2000). *Chemical constituents investigation on Tetrastigma hemsleyanum, T. hypoglaucum and Cypripedium tibeticum*. Peking Union Medical College. PhD Thesis of Master Degree.
Liu, D. D., Cao, G., Zhang, Q., Ye, Y. L., Han, L. K., & Ge, W. H. (2015). Inhibition effect of flavonoids from *Radix Tetrastigmae* on acute lung injury of aged mice through p38MAPK and NF-κB pathway. *Chinese Pharmacological Bulletin, 31*(12), 1725–1729.
Liu, D., Ju, J. H., & Lin, G. (2002). New sylflavones from *Tetrastigma hemsleyanum* (Vitaceae). *Acta Botanica Sinica, 44*(2), 1–23.

Liu, J. T. (2019). *Discovery of antiviral drugs Tetrastigma hemsleyanum Diels et Gilg and study on its mechanism*. Shandong University of Traditional Chinese Medicine. PhD Thesis of Master Degree.
Liu, P. G., & Wei, K. M. (2018). Research progress in the biology, pharmacology and clinical application of Sanyeqing. *Chinese Journal of Traditional Medical Science and Technology, 25*(06), 927–932.
Lu, X. L. (2001). Qigui Qianjinba decoction for the treatment of 80 cases of arthralgia syndrome by internal and external use. *Chinese Folk Therapy, 9*(01), 20–21.
Lv, X. K., Wang, P., & Chen, J. B. (2014). Effect of Sanyeqing Sanjie Kang' ai Formula on pathological complete response rates in triple-negative breast cancer patients undergoing neoadjuvant chemotherapy. *Journal of Traditional Chinese Medicine, 55*(23), 2016–2019.
Pan, Q. D., Xiong, Y. Y., Chen, W. D., Du, Q. H., & Li, J. J. (2012). Extraction technology and antioxidant activity of total flavonoids and total triterpenoids from *Tetrastigma planicaule*. *Chinese Journal of Traditional Chinese Medicine, 35*(10), 1679–1683.
Pan, Q. D., Xiong, Y. Y., Chen, W. D., Du, Q. H., & Meng, Q. Y. (2013). Antioxidant activity of different polarity chemical constituents from *Tetrastigma planicaule*. *Chinese Journal of Experimental Medical Formulae, 19*(1), 232–235.
Qian, L. H., Dai, D. L., Jiang, H. Y., & Lin, W. H. (2015). Research progress on the endangered medicinal plant Sanyeqing. *Journal of Zhejiang Agricultural University, 27*(7), 1301–1308.
Qiu, M. C., Xu, Z. J., & Yang, Z. J. (2018). Study on the effect of different extracts from *Radix Tetrastigme* on antitumor cells. *Modern Distance Education of Chinese Medicine, 16*(017), 93–95.
Qiu, M. C., Zhou, Z. D., & Yang, Z. J. (2019). Total flavonoids from *Tetrastigma hemsleyanum* Diels et Gilg induce apoptosis of breast cancer cells through MAPK pathway. *The Chinese Journal of Clinical Pharmacology, 35*(23), 3059–3063.
Rao, R. F., Lv, W. D., Ni, C. Z., & Zhu, J. (2016). Determination of monosaccharides in polysaccharides of *Tetrastigmatis hemsleyani* by ion chromatography-pulsed amperometric detection. *Asia-Pacific Traditional Medicine, 12*(12), 42–44.
Ru, Y., Chen, X., Wang, J., Guo, L., Lin, Z., Peng, X., et al. (2019a). Polysaccharides from *Tetrastigma hemsleyanum* Diels et Gilg: Extraction optimization, structural characterizations, antioxidant and antihyperlipidemic activities in hyperlipidemic mice. *International Journal of Biological Macromolecules, 125*, 1033–1041.
Ru, Y., Chen, X., Wang, J., Guo, L., Lin, Z., Peng, X., et al. (2019b). Structural characterization, hypoglycemic effects and mechanism of a novel polysaccharide from *Tetrastigma hemsleyanum* Diels et Gilg. *International Journal of Biological Macromolecules, 123*, 775–783.
Ru, Y., Chen, X., Xu, J., Huang, L., Jiang, M., Guo, L., et al. (2018). Hypoglycemic effects of a polysaccharide from *Tetrastigma hemsleyanum* Diels & Gilg in alloxan-induced diabetic mice. *Chemistry & Biodiversity, 15*(08) e1800070.
Shao, J. C. (2011). *Studies on the chemical constituents of Tetrastigma planicaule (Hook.) Gagnep*. Jinan University. Thesis of Master Degree.
Shao, J. C., He, C. H., Lei, T., Hong, A. H., & Cen, Y. Z. (2010). Chemical constituents of *Tetrastigma planicaule* (HooK) Gagnep. *Chinese Pharmaceutical Journal, 45*(021), 1615–1617.
Shi, G. R. (2012). *Study on the bioactive chemical constituents of Tetrastigma obtectum (Wall.) Plan*. Tianjin Medical University. PhD Thesis of Master Degree.
Song, B. Z., & Wan, D. R. (2003). Survey of commonly used botanicals (Vitisaceae) of Tujia Nationality in Hubei Province. *Chinese Journal of Ethnomedicine and Ethnopharmacy, 61*, 117–118.
Sun, C. L., Wu, H., Lou, T. L., Zhang, L. X., Zhang, Y. J., & Peng, X. (2018). UPLC-Q-TOF-MS method for analysis of some chemical components in the ground of *Tetrastigma hemsleyanum*. *Chinese Traditional Patent Medicine, 40*, 1424–1429.
Sun, L. (2018b). *Study on the directed screening of vascular targeted active ingredients of T. hemsleyanum and its influences on tumor angiogenesis*. Zhejiang A&F University. Thesis of Master Degree.
Sun, Y. (2018a). *Chemical composition, activities of antioxidation and anticancer of Tetrastigma hemsleyanum Diel et Gilg*. Nanchang University. Thesis of Master Degree.
Sun, Y., Li, H. Y., Hu, J. N., Li, J., Fan, Y. W., Liu, X. R., et al. (2013). Qualitative and quantitative analysis of phenolics in *Tetrastigma hemsleyanum* and their antioxidant and antiproliferative activities. *Journal of Agricultural and Food Chemistry, 61*, 10507–10515.
Sun, Y., Qin, Y., Li, H. Y., Peng, H., Chen, H. B., Xie, H. R., et al. (2015). Rapid characterization of chemical constituents in *Radix Tetrastigma*, a functional herbal mixture, before and after metabolism and their antioxidant/antiproliferative activities. *Journal of Functional Foods, 18*, 300–318.
Sun, Z. Y., Kong, Y., & Li, L. (2021). Yu Jingmao's experience in the treatment of recurrent suppurative tonsillitis in children. *Journal of Pediatrics of Traditional Chinese Medicine, 17*(03), 16–19.
Wang, B. (2020). *RTP affects the proliferation, migration and invasion of liver cancer cells by down-regulation the expression of miR-151*. Shanxi Medical University. Thesis of Master Degree.
Wang, B., Cheng, Y. F., Wu, J., Li, G. L., & Wang, S. M. (2020). Effects of polysaccharides from roots of *Radix Tetrastigma* on proliferation, apoptosis, migration and invasion of HepG2 cells. *Journal of Jinan University (Natural Science & Medicine Edition), 41*(05), 444–454.
Wang, C.Y., Jang, H. J., Han, Y. K., Su, X. D., Lee, S. W., Rho, M. C, Wang, H. S, Yang, S. Y, Kim, Y. H. (2018). Alkaloids from *Tetrastigma hemsleyanum* and their anti-inflammatory effects on LPS-induced RAW264.7 cells. *Molecules*, *23* (6),1445.
Wang, D. D., Gao, R., & Yan, B. (2019). Experimental study on the effects of *Radix Tetrastigmae* on respiratory syncytial virus. *Natural Product Research and Development, 31*(006), 1070–1074.
Wang, H., Sun, B. F., Ji, Y. D., Yu, Y. S., Zang, G. Y., Chen, M., et al. (2017). Protective effects of Miao medicine *Tetrastigma hypoglaucum* Planch on myocardial ischemia reperfusion injury in rats. *Journal of Liaoning University of Traditional Chinese Medicine, 44*(12), 2649–2651.
Wang, H., Sun, B. F., Ji, Y. D., & Peng, Z. P. (2016). Study on the antibacterial activity of *Tetrastigma hypoglaucum* Planch. *Medical Information, 29*(18), 137–138.
Wang, J., Guo, W. L., Yang, D. F., Xue, Y. D., Xu, X. H., & Liang, Z. S. (2015). The research development of a rare medicinal plant: *Tetrastigma hemsleyanum* Diels et Gilg. *Bulletin of Botanical Research, 4*, 39–46.
Wang, J., & Peng, X. (2015). Apoptosis of human intrahepatic cholangiocarcinoma cells (HCCC-9810) induced by the extract from *Tetrastigma hemsleyanum*. *Chinese Pharmacist, 9*(07), 13–17.
Wang, M. Y., Chen, W. F., Chen, Y., & Wei, K. M. (2014). Study on inhibition effect of ethylacocate extract of *Tetrastigma hemsleyanum* Diels et. Gilg on transplantation tumor by human hepatocarcinoma cell HepG-2 in athymic mouse. *China Traditional Chinese Medicine Science and Technology, 21*(02), 157–158.
Wang, Y., Zhang, S. P., & Yu, Z. (2018). b). Effect of the extract of *Radix Tetrastigmatis* on the function of NK cells *in vitro*. *Journal of Medical Research, 44*(12), 155–159.
Wei, K. (2007). Study on the anti-tumor mechanism and the clinical application of *Tetrastigma hemsleyanum* Diels et. Gilg. *Journal of Medical Research, 36*(11), 41–43.
Wei, M. J., Chen, Z. L., Pu, J. B., Wei, K. M., & Liu, P. G. (2018). MiRNA regulation effect of *Radix Tetrastigma Hemsleyani* flavone against lung cancer cell A549 based on endocytosis pathway. *Chinese Journal of Traditional Medical Science and Technology, 25*(05), 661–665.
Wu, H. Y., Wu, Y. T., Chen, Y. Y., Luo, H. L., & Jiang, H. F. (2019). Effect of *Radix Tetrastima hemsleyani* flavone on apoptosis and MAPK signaling pathway in myeloid leukemiao NB-4 cells. *Chinese Journal of Pathophysiology, 35*(08), 1451–1456.
Wu, Q. (2021). Effect and mechanism research of cloverleaf flavonoids regulated STAT3 signaling pathway on proliferation and apoptosis of bladder cancer cells. *China Modern Doctor, 59*(17), 25–28.
Xia, G. S., Li, S. H., & Zhou, W. (2018). Isoquercitrin, ingredients in *Tetrastigma hemsleyanum* Diels et Gilg, inhibits hepatocyte growth factor/scatter factor-induced tumor cell migration and invasion. *Cell Adhesion & Migration, 12*(5), 464–471.
Xing, Q. (2020). *Screening and mechanism of anti-inflammatory components in Tetrastigma hemsleyanum targeting transcription factor Nrf2*. Nanchang University. thesis of Master Degree.
Xing, Q., Zheng, L. F., Gan, T., Xiao, T., Deng, Z. Y., & Liu, X. R. (2020). Anti-inflammatory effect and mechanism of major components in *Tetrastigma hemsleyanum* Diels et Gilg. *Food & Machinery, 36*(5), 9.
Xu, C. J., Ding, G. Q., Fu, J. Y., Meng, J., Zhang, R. H., & Lou, X. M. (2008). Immunoregulatory effects of ethyl-acetate fraction of extracts from *Tetrastigma hemsleyanum* Diels et. Gilg on immune functions of ICR mice. *Biomedical and Environmental Sciences, 21*(4), 325–331.
Xu, S., Jin, P., Hui, H., & Tang, S. (2017). Study on the chemical constituents of the petroleum ether fraction from *Tetrastigma hemsleyanum*. *Northwest Pharmaceutical Journal, 32*(03), 270–272.
Xu, W., Fu, Z. Q., Lin, J., Huang, X. C., Chen, D., Yu, H. M., et al. (2014). Qualitative and quantitative analysis of main components of *Tetrastigma hemsleyanum* by HPLC-Q-TOF-MS and UPLC-QqQ-MS. *Journal of Chinese Materia Medica, 39*, 4365–4372.
Xu, Y. S. (2006). Treatment of 72 cases of infantile exogenous fever with Sanye Qingshi Shitang. *Journal of Practical Traditional Chinese Medicine, 22*(7), 412.
Xu, Y., He, Y. Z., & Shi, K. J. (2015). Clinical experience of SHI Kui-jun in treating malignant lymphoma. *China Journal of Traditional Chinese Medicine and Pharmacy, 30*(4), 1110–1112.
Yang, X. Z., & Wu, J. (2009). A study of anti-HBV activity of extract of *Radix Tetrastigmae*. *Journal of Nanjing University of Traditional Chinese Medicine, 25* (004), 294–296.
Yin, Z., Wen, Q., & Cai, D. Z. (2020). Extraction and antioxidant activity of polysaccharides from *Tetrastigma hemsleyanum*. *Northern Horticulture, 2020* (22), 96–103.
Yuan, Y., Zhu, B. X., Liu, J. Q., Zhou, Y., Lv, X. T., Zhong, H., et al. (2016). Effect of the water extract of *Tetrastigma hemsleyani* on the cytotoxic activity of NK cells against gastric cancer cell lines BGC-823. *Journal of Gastroenterology and Hepatology, 25*(006), 633–663.
Zeng, M. L., Shen, N. T., Wu, S. W., & Li, Q. (2017). Analysis on chemical constituents in *Tetrastigma hemsleyanum* by UPLC-Triple-TOF/MS. *Chinese Herbal Medicines, 48*(05), 874–883.
Zeng, T. (2013). *Research on the chemical constituents of the Shi Hou Zi*. Gannan Normal University. Thesis of Master Degree.
Zhang, J. J., Zhang, Z. F., Lv, G. Y., Lu, M. D., & Fang, L. L. (2021). Comparison between root and shoot antioxidant activity of *Tetrastigma hemsleyanum*. *Journal of Zhejiang Agricultural Sciences, 62*(04), 709–711.
Zhang, L. Y., Ke, J. H., Qiu, Z. Y, et al. (2016). A prescription of external Chinese medicine for the treatment of rheumatism. CN105521224A.
Zhang, Q. Q., & Feng, Z. Q. (2019). Effect of flavonoid extract from *Radix Tetrastigme* on PGE2 and COX-2 in spleen mononuclear cells of lewis lung carcinoma mice. *Zhejiang Journal of Integrated Traditional Chinese and Western Medicine, 27*(10), 842–845.
Zhang, Q., Lu, R. M., Chen, S. B., & Li, B. (2019). Research progresses of *Tetrastigma planicaule* (Hook.) Gagnep and same generic plants. *Guiding Journal of Traditional Chinese Medicine and Pharmacy, 25*(19), 121–126.

Zhao, F., Morita, I., Murota, S. I., & Yao, X. S. (1999). Anti-inflammatory activities of *Phyllanthus emblica* and *Betula alnoides* through transcription factor NF-κB pathway. *Hemo Yixuexiong Mushroom, 16*, 155–162.
Zhao, J., Shi, G. R., & Duan, H. Q. (2020). Isolation of antitumor metastasis indole alkaloids from *Tetrastigma obtectum*. *Journal of Tianjin University of Traditional Chinese Medicine, 39*(06), 690–694.
Zhong, L. R., Chen, H., Jing, J., Qiao, H. L., Wei, K. M., & Wang, W. D. (2017). *Radix Tetrastigma hemsleyani* flavone suppresses human lung carcinoma A549 cell via proteasome inhibition. *Chinese Journal of Clinical Pharmacology and Therapeutics, 22*(010), 1123–1126.
Zhou, X. M. (2013). Treating 228 cases of chronic hepatitis B treated with Hugan Toudu decotion. *Clinical Research of Traditional Chinese Medicine, 5*(24), 66–67.
Zhu, B., Qian, C., Zhou, F., Guo, J. J., Chen, N. P., Gao, C. X., et al. (2020). Antipyretic and antitumor effects of a purified polysaccharide from aerial parts of *Tetrastigma hemsleyanum*. *Journal of Ethnopharmacology, 253*(18) 112663.