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Review

Prevention and treatment of radiation injury by traditional Chinese medicine: A review

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ABSTRACT

Nuclear radiation exposure events and tumor radiotherapy are highly susceptible to a range of psychological, physiological and other health problems, which can seriously affect patients' quality of life. It has been shown that 87.5 % of tumor patients are exposed to varying degrees of radiation injury during radiotherapy. The treatment of radiation injury (RI) in modern medicine is limited to drug therapy, cell therapy, etc. Among them, the most chemical drugs cause many adverse reactions including fatigue, nausea, vomiting, etc., and there are very few drugs dedicated to the treatment of RI. Traditional Chinese medicine (TCM) is a rich natural medicinal resource, which has a wide range of pharmacological activities, multiple targets of action and minimal toxic side effects. Many studies have demonstrated that TCM and its compound preparations have enormous potential in the treatment of radiation induced comprehensive diseases. However, TCM is limited in clinical application due to its slow onset of action, complex active ingredients, and low bioavailability. Therefore, the article reviews the application, molecular mechanisms, and new dosage forms of TCM in the prevention and treatment of RI. On this basis, we will focus on discussing the development advantages and application prospects of the combination of traditional Chinese and Western medicine to achieve highly efficient treatment of RI. This review aims to provide scientific and effective drug delivery strategies and basic theoretical support for the clinical effective treatment of RI with TCM, and further promote the innovative development of TCM.

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1. Introduction

Since a number of nuclear accidents (e.g., Chernobyl nuclear accident and Fukushima nuclear meltdown) and the launch of Japan's nuclear contaminated water discharge event with a projected discharge time of up to 30 years in 2023, a series of radiation damage health problems such as cancer, genetic damage, and various organ and skin injuries caused by radioactive substances in nuclear contamination have become the focus of worldwide attention and one of the hot issues in today's society (Aronova, 2019). Severe radiation injury (RI) can even cause multi-tissue and organ failure, ultimately leading to the death of the organism (Allen, Her, & Jaffray, 2017; Nanduri, Duddempudi, Yang, Tamarat, & Guha, 2021). Currently, with the development of nuclear medicine, radiation therapy occupies an important position in the comprehensive treatment of tumors. However, the common complication of radiation tissue injury limits the current development of radiotherapy. According to the statistics, RI of varying degrees occurs in 87.5 % of patients with soft-tissue sarcomas treated with radiation therapy (Koeksal et al., 2023). Another report states that about 95 % of patients develop radioactive skin damage after radiotherapy (Wang et al., 2024). At present, there is no systematic standardized treatment program for RI. The main treatment methods of RI include drug prevention and treatment, cell therapeutics and gene therapy (Liu, Liang, Ma, Li, & Liu, 2023; Yang et al., 2024). Among them, most of the drugs currently in clinical use are chemical and biological agents (Liu, Liang, Ma, Li, & Liu, 2023), but most of them have serious side effects and expensive defects. For example, amifostine is a commonly used radiation protection agent, but it can cause adverse reactions such as nausea, vomiting, hypotension and drowsiness (Ji et al., 2023). In addition, currently the only drugs approved by the FDA for treating RI are Neupogen, Neulasta, Leucine, and Nplate (Satyamitra, Cassatt, & Taliaferro, 2021). Therefore, there is a shortage of drugs and an urgent need to find effective therapeutic drugs for RI.

It is well known that the biological effects exhibited by the body vary depending on the duration and dose of radiation exposure. Acute radiation syndrome may result from receiving large doses of radiation over a short period of time. The study showed that doses of ionizing radiation in the range of 1–7 Gy cause damage to the human hematopoietic system, while radiation doses greater than 8 Gy also cause gastrointestinal syndrome (Kiang & Olabisi, 2019). Another study noted that low-dose radiation mediation is involved in biological effects such as oxidative stress and DNA damage, and low-dose exposures often cause chronic radiation damage (Shin et al., 2020). While the etiology of RI is clear, its specific mechanism is a complex process. On the one hand, radiation exposure has the potential to inflict damage on crucial biological macromolecules, including cellular nucleic acids, proteins, and lipids (Zhou, et al., 2018a). Among them, radiation exposure can directly or indirectly cause DNA damage to varying degrees, including base damage, single-strand breaks and double-strand damage (Gong, Zhang, Liu, Zhang, & Han, 2021; Wilkinson, Hill, & Parsons, 2023). DNA double-strand damage activates the ataxia telangiectasia mutated (ATM), which in turn activates *p53* gene, leading to apoptosis and a host of other biological effects (Okazaki, 2022). On the other hand, radiation irradiation leads to excessive production of free radicals and reactive oxygen species (ROS) in cells, which can lead to mitochondrial dysfunction and disrupt the body's oxidative homeostasis system (Wei et al., 2019). Excessive ROS may lead to the generation of sustained oxidative stress, severe DNA damage, and a variety of cellular responses, including cell cycle arrest, senescence, and apoptosis (Xu et al., 2021). Their combined action can further lead to cell injury or apoptosis, which in turn triggers a series of biological effects such as oxidative stress, inflammatory responses and even fibrosis of tissues and organs (Fig. 1). In addition, it has been suggested that gut microbiota not only occurs in radiation-induced intestinal injury, but also involves in mediating various different forms of RI (Wang, Cui, Nie, Sun, & Zhang, 2023).

Traditional Chinese medicine (TCM) has a good effect and a long history in treating diseases in China. It has been proved that most of the TCM have strong potential for the prevention and treatment of RI (Zhang, 2021a; Zhang, et al., 2021b). Currently, a diverse array of TCM formulations, including active ingredients (flavonoids (Wang et al., 2020b), curcumin (Ghanbarzadeh et al., 2023) and astragaloside IV, etc.), total alkaloids of *Stephaniae Cepharantha Radix* (Li et al., 2024) and preparations such as Yiqi Jiedu Tang (Zhang, et al., 2022a; Zhang, et al., 2022b), Danggui Buxue Tang (Huang, Cheng, Wang, Dong, & Gao, 2022), etc., has been developed to provide a rich resource for new anti-RI drugs to be developed. The main therapeutic ideas of TCM are clear away heat and detoxification, benefit *qi* and nourish *yin*, etc., with the ultimate goal of getting rid of the toxic side effects of radiation, promoting the repair of damage, and enhancing the recovery of the body's own immunity (Yang, Li, Yang, & Wu, 2021). At present, many TCM preparations have been reported in the treatment of RI in clinical practice, but most of them have not elucidated the material basis and mechanism of their therapeutic effects (Zhou et al., 2023). The review summarizes the pathogenesis, molecular mechanisms, pharmacological effects, and applications of TCM in the prevention and treatment of RI, with a focus on exploring the potential application of novel dosage forms of TCM in radiation therapy, which provides a reference for the development and clinical application of TCM in RI therapy.

2. TCM etiology and pathogenesis of RI

With the development of nuclear technology, it is only in recent times that the understanding of RI in TCM has been further researched. The study pointed out that the effect of RI on the organism is consistent with the TCM characteristic of causing disease by toxicity. Therefore, TCM considers radiation to be a special kind of toxicity (Gao et al., 2016). The pathogenic characteristics of

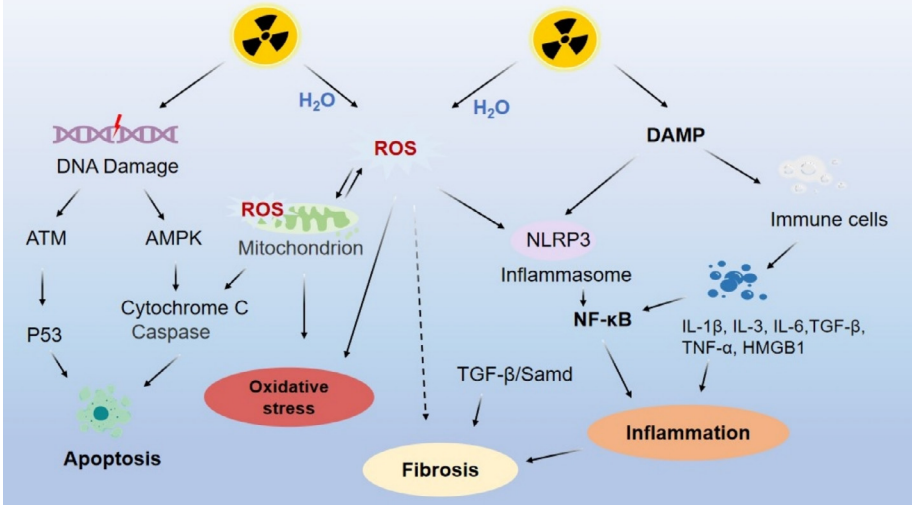

Fig. 1. Pathogenic mechanisms of radiation injury. AMPK: AMP-activated protein kinase; DAMP: damage-associated molecular pattern; NLRP3: pyrin domain-containing protein 3; NF-κB: transcription factor nuclear factor-κB; IL-1β: interleukin 1β; IL-3: interleukin 3; IL-6: interleukin 6; TGF-β: transforming growth factor-β; TNF-α: tumor necrosis factor alpha; HMGB1: high mobility group box 1.

the radiation toxicity include virulence, internal damage, persistence and transmissibility (Zhang & Li, 2019). When radiation toxicity invades the human body, it can cause a serious imbalance between *yin* and *yang* due to excess evil energy and insufficient sources of *qi* and blood, which ultimately leads to symptoms of systemic *qi* and *yang* (Li et al., 2020). Feng et al. analyzed the characteristics of TCM syndromes through the acute radiation injury model in rats. (Feng et al., 2018). It is believed that acute radiation injury is syndrome of intense heat toxin, vigorous heat of *qi* and *ying* type in the early stage, in the middle stage is original *qi* deficiency and damage, binding of blood stasis and toxin syndrome, and in the late stage is *qi* and blood deficiency, blood stasis and collateral obstruction syndrome (Feng et al., 2018).

Another study pointed out that, according to TCM theory of "conghua (It means that the radiation toxicity can be transformed into *yang* or *yin* poison after invading the organism, which leads to the damage of the organism.)" and "chuanshe (It refers to the radiation toxicity through a specific pathway or way, gradually damage other organs and tissues of a dynamic pathological evolution.)", after invading the human body, radiation toxicity can be sublimated into *yang* or *yin* toxicity (Xie et al., 2023; Zhao, Hu, Jin, Sun, & Chen, 2023). It is carried by "*qi*", which is transmitted through the exterior and the interior, the five elements, and the meridians and collaterals (Xie et al., 2023; Zhao, Hu, Jin, Sun, & Chen, 2023). Eventually, the radiation toxicity can lead to varying degrees of tissue damage and even multiple organ failure and death by spreading to all tissues of the body. In recent years, studies have shown that radiation damage is closely related to injury of the "spleen" in TCM, which is considered to be the guardian of the spleen, and can exercise the ability to defend itself. Radiation toxicity invade the body, injuring the guards of the spleen and triggering different degrees of damage to the body (Wang, Wang, & Hu, 2021). It can be seen that radiation poisonous evil disease has a certain complexity, and the etiology and pathogenesis of different injuries are different.

Therefore, the main TCM etiology and pathogenesis of RI can be summarized as follows. At present, TCM generally considers radiation to be a kind of toxicity. At the initial stage, radiation poisoning invades the body, resulting in deficiency of healthy *qi* and overabundance of pathogenic *qi*, which further passes through the "conghua" and "chuanshe", injuring the spleen's guards and upsetting the balance of *yin* and *yang* in the body. In addition, RI is mostly considered to be due to toxin pathogen causing disease, binding of heat and toxicity, contention between heat and stasis (Wu & Li, 2023), ultimately leading to the body's disharmony between *yin* and *yang*, *qi* and *yin* deficiency syndrome, etc.

There is no common standard for the dialectical typing of RI in TCM, and the analysis is mainly based on the patient's clinical manifestations. For example, some studies have analyzed that there are nine TCM syndrome names for radioactive skin injury after standardization. Among them, the frequency of the Evil-Heat Blazing Certificate was as high as 96.92 % (Wu, Liao, Kang, Li, & Song, 2021). In further analysis of the medication pattern of TCM, the frequency of the use of heat-clearing herbs was the highest at 44.64 %, followed by medicines for deficiency tonic medicines, purgative herbs and blood-activating and stasis-resolving medicine (Wu et al., 2021). Thus, the principle that the main treatment of RI should be based on clearing heat and resolving toxins, supplemented by medicines that boost *qi* and nourish *yin* and activate blood circulation and remove blood stasis, was put forward (Gu, Zhou, & Shi, 2020; Yang, Li, Yang, & Wu, 2021) (Fig. 2). It removes the harmful effects of radiation poisoning on the human body and restores the positive energy of the organism. Commonly used TCMs include heat-clearing and detoxifying medicines such as *Scutellariae Radix* (Huangqin in Chinese), *Polygoni Cuspidati Rhizoma* et *Radix* (Huzhang in Chinese), etc. Qi-benefiting and yin-supplementing medicines such as *Astragali Radix* (Huangqi in Chinese), *Lycii Fructus* (Gouqizi in Chinese) and *Ophiopogonis Radix* (Maidong in Chinese), etc. Blood-stasis-activating medicines such as *Curcumae Longae Rhizoma* (Jianghuang in Chinese), *Salviae Miltiorrhizae Radix* et *Rhizoma* (Danshen in Chinese). There are also other TCMs that aim to detoxify the body, regulate *qi* and blood, and promote the recovery of the patient's bodily functions.

3. Molecular mechanisms of TCM for anti-RI

TCM has been shown to inhibit oxidative stress damage, anti-inflammatory, prevent and repair DNA damage, and enhance immune system function.

3.1. Inhibiting oxidative damage

Radiation can lead to excessive intracellular production of ROS and mitochondrial dysfunction and reduced glutathione (GSH)

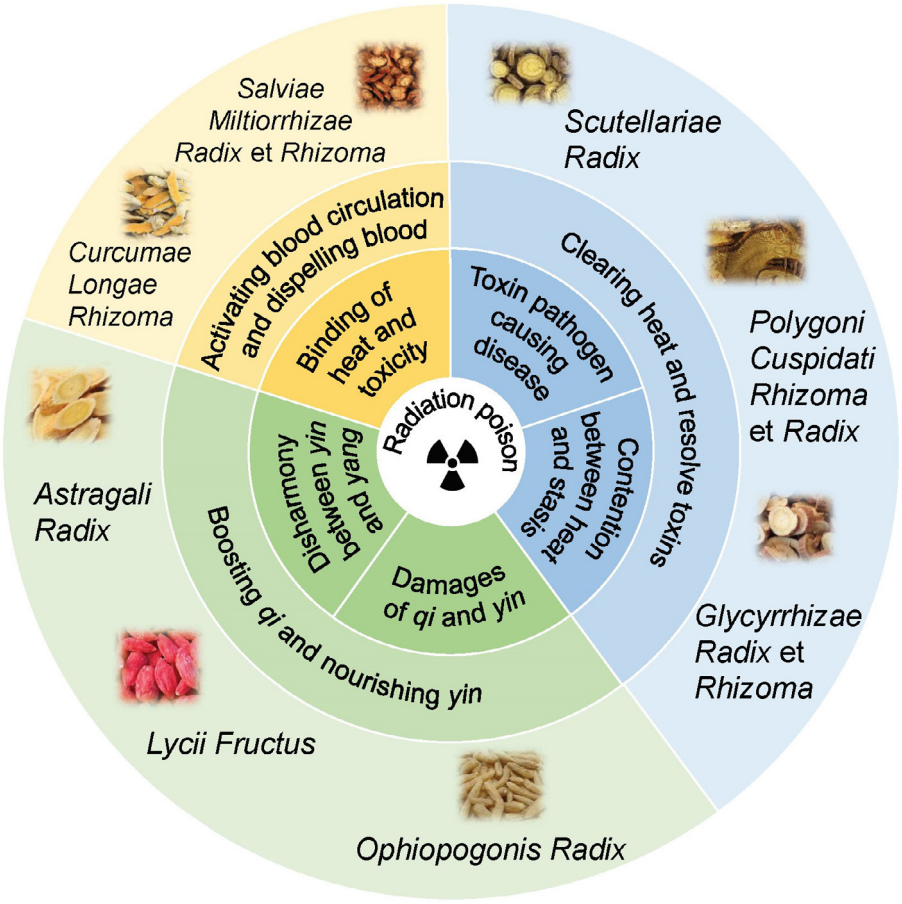

Fig. 2. Etiology and pathogenesis of TCM for radiation injury.

synthesis, which can lead to oxidative stress-induced damage in cells (Yang, Luo, et al., 2021). Meanwhile, mitochondrial damage generates excess ROS, which attack the mitochondria causing a vicious cycle that leads to a sustained oxidative stress response. This is one of the main reasons for the worsening of RI. In addition, ROS are involved in mediating DNA damage, apoptosis and autophagy in cells (Shrishrimal, Kosmacek, & Oberley-Deegan, 2019).

A large number of studies have shown that TCM can inhibit radiation-induced oxidative stress, thereby reducing oxidative damage. It is mainly through scavenging excessive ROS, enhancing the activities of various antioxidant enzymes in the body, and regulating related signaling factors and pathways. These herbs include *Croci Stigma* (Xihonghua in Chinese) and *Lycii Fructus*, etc. On the basis of clearing ROS, *Croci Stigma* and *Acanthopanacis Senticosi Radix* et *Rhizoma* seu *Caulis* (Ciwujia in Chinese) can enhance the activity of antioxidant enzymes superoxide dismutase (SOD), catalase (CAT), malondialdehyde (MDA) and GSH, and enhance the antioxidant capacity of the body (Song et al., 2022; Zhang et al., 2020a). *Lycium barbarum* polysaccharide-glycoprotein may maintain the stability of mitochondrial membrane potential, activates nuclear factor erythroid 2-related factor 2 (Nrf2) and downstream pathways, inhibits oxidative stress and iron death, and reduces radiation-induced cell death (Jiang, Xiao, Li, & Mu, 2023).

3.2. Regulating inflammatory response

It is well known that inflammation is one of the typical clinical features of RI. Overaccumulation of ROS and impairment of the oxidative homeostasis system during the above processes can trigger chronic inflammation. Irradiation causes an increase in the number of macrophages and T-lymphocytes in the organism, a phenomenon that induces the release of a variety of inflammatory mediators (e.g. NF-κB and SMAD2/3) and cytokines (Yahyapour et al., 2018). At the same time, irradiation-induced cellular damage and death lead to the release of damage-associated molecular pattern (DAMP) molecules from the cells, which in turn leads to the accumulation of various immune cells and the accumulation of multiple cytokines leading to inflammation (Li, et al., 2023a; Yamaga, Aziz, Murao, Brenner, & Wang, 2024; Zhang et al., 2021b).

TCM has a significant therapeutic effect on radiation-induced inflammation. On the one hand, it can inhibit the secretion release or expression of relevant inflammatory factors and reduce the infiltration of inflammation to prevent further deterioration of inflammation caused by irradiation, or even the occurrence of fibrosis in tissues and organs in chronic injury. On the other hand, it can attenuate the inflammatory response by modulating various inflammation-related pathways such as HMGB1/Toll-like receptor 4 (TLR4), mitogen-activated protein kinases p38 (MAPKp38)/Nrf2 (Xiao et al., 2020), and NF-kB/TGF-β (Hassan, Moustafa, EL-Khashab, & Mansour, 2021). Most of the TCMs have both of these effects. For example, *Amomi Fructus* (Sharen in Chinese) could enhance the expression of Nrf2 and its target genes and antioxidant genes such as *heme oxygenase-1* (*HO-1*), and inhibit the release of pro-inflammatory cytokine levels (Drishya, Dhanisha, Raghukumar, & Guruvayoorappan, 2023a; Drishya et al., 2023b).

3.3. Preventing and repairing DNA damage

DNA is highly sensitive to radiation, and lower doses of radiation can directly or indirectly cause significant DNA lesions. Signals

of DNA injury may cause cell cycle disorders and trigger apoptosis or necrosis, which in turn leads to cell death. It can also lead to genetic mutations, which can lead to the development of genetic diseases or cancer (Shimura, 2023). Phosphorylated histone H2AX (γ-H2AX) is considered to be one of the important markers of DNA damage because it will accumulate at the damage site and recruit repair proteins to repair DNA after DNA injury (Wang, Zhi, & Li, 2020).

TCM such as *Ginseng Radix* et *Rhizoma* (Renshen in Chinese) and Yi Qi Jie Du (YQJD) decoction have better therapeutic effects on radiation-induced DNA damage. It was found that the expression of γ-H2AX was significantly reduced in the irradiated mouse model pretreated with *Ginseng Radix* et *Rhizoma* and YQJD by measuring γ-H2AX in mouse cells, which proved that they could prevent or promote DNA damage repair (Zhang, Zhang, Liang, Tang, & Wei, 2023; Zhang, et al., 2022b). In addition, YQJD could also promote DNA damage repair through the non-homologous end-joining (NHEJ) pathway (Zhang et al., 2022b).

3.4. Enhancing the immune system

The damage to the immune system caused by radiation contributes to a significant reduction in the body's ability to recover itself. It is well known that TCM are effective in regulating the body's functions and regulating the immune system. The spleen is the largest peripheral immune organ and it is highly sensitive to radiation. Studies have shown that YQJD can reduce the apoptosis of splenic lymphocytes, protect the structure and function of the spleen, and at the same time maintain the balance of Th1/Th2 (T helper cell) and Th17/Treg (regulatory T cell) to ensure a normal immune response (Wang, et al., 2022a). TCM *Lycii Fructus* can effectively prevent the decline in the percentage of lymphocytes after radiation damage, activate macrophages to enhance the body's immunity, and promote the expression of cytokines TNF-α, IL-1β, IL-6 and IL-12 (Zheng et al., 2021).

4. Research progress of TCM for anti-RI

Studies have shown that single herbs (Table 1) and prescriptions (Table 2) of TCMs demonstrate anti-RI potential. These are discussed as follows.

4.1. Single herbs

4.1.1. TCM for heat-clearing and detoxifying

The heat-clearing and detoxifying herbs *Scutellariae Radix* and *Polygoni Cuspidati Rhizoma* et *Radix* have the effect of clearing away fire-heat and toxins. The modern research shows that they have good anti-inflammatory effects (Wang et al., 2018). This type of TCM can clear the radiation toxicity and improves the radiation-induced inflammatory reaction, etc. *Scutellariae Radix* is a TCM with the effects of clearing heat and drying dampness, purging fire and removing toxin. Its research has shown that it possesses a wide range of modern pharmacological activities such as antioxidant, anti-inflammatory and immunomodulation (Li, Liu, & Qin, 2022). Baicalin is one of the main active components of *Scutellariae Radix*, and studies have demonstrated that baicalin could eliminate excessive ROS and affect the NF-κB pathway (Kumar Maurya & Lomte, 2022). Another study noted that it inhibited the overproduction of several cytokines including TGF-β, TNF-α, IL-6 and IL-1β, and inhibited the cysteinyl leukotrienes (CysLTs)/type 1 CysLT receptors (CysLT1) pathway, which alleviated radiation lung inflammation and fibrosis (Bao et al., 2022). Another herb, *Glycyrrhizae Radix* et *Rhizoma* (Gancao in Chinese), is the most commonly used herb in Chinese medicine compounding, which can clear heat and resolve toxins and tonify middle and replenish *qi*. Glycyrrhizin (GL) is one of its most important bioactive components, with a variety of pharmacological effects such as anti-inflammatory, anti-oxidant, anti-cancer activity and the regulation of immunity (Bakr, Shao, & Farag, 2022; Zhang et al., 2023). Studies have shown that GL is a natural inhibitor of HMGB1. It inhibits the increase of TNF-α, IL-1β and IL-6 inflammatory factors and ameliorates radiation-induced inflammation and lung injury by modulating the inhibition of the HMGB1/TLR4 pathway (Zhang et al., 2020e; Zheng et al., 2020). In addition, glycyrrhetinic acid, a metabolite of GL, was shown to ameliorate radiological pulmonary fibrosis (Chen et al., 2024).

In addition, *Polygoni Cuspidati Rhizoma* et *Radix* could excessive ROS while inhibiting the phosphoinositide 3-kinase (PI3K)/the serine-threonine protein kinase (AKT)/mammalian target of rapamycin (mTOR) pathway, alleviating the body's oxidative stress and preventing the development of fibrosis in mice with radiological lung injury (Chen et al., 2023; Gao et al., 2022). Another study noted that it also regulates the HO-1 pathway and improves the body's antioxidant function (Guo et al., 2020).

4.1.2. Tonifying TCM

Tonic Chinese medicines, also known as deficiency tonics, have the effect of benefiting *qi* and nourishing *yin*. *Astragali Radix*, *Lycii Fructus* and other tonic herbs can be used to treatment of irradiation-induced disharmony between *yin* and *yang*, *qi* and *yin* deficiency syndrome. *Astragali Radix* has the effect of *qi* replenishing and surface solidifying, sore healing and muscle generating. It has a variety of modern pharmacological activities such as immunomodulation, antiviral activity and antioxidant activity (Li, Liu, & Qin 2022). It was noted that astragalus polysaccharides reduced radiation-induced ROS production and regulated the expression of apoptotic proteins in radiation bystanders (Zhang, et al., 2020f). It can also prevents radiation-induced oxidative stress and reduces apoptosis by inhibiting the mitochondrial/Caspase-3 pathway (Xu et al., 2019). Moreover, it was found that Astragaloside IV could activate the brain-derived neurotrophic factor (BDNF)/tropomyosin-related kinase receptor B (TrkB) pathway (Liu, et al., 2023b). Meanwhile, it could alleviate radiation-induced inflammation and damage by inhibiting cellular iron death (Chen & Wu, 2023). These studies provide strong evidence for the antiradical properties of *Astragali Radix*.

Lycii Fructus is one of the traditional medicinal and food herbs that play an important role in anti-inflammation, immunomodulation and promoting gut health (Qiang et al., 2023). In recent years, it has been found that *Lycii Fructus* have a good therapeutic effect on RI, and the potential mechanisms are discussed in the following. *Lycium barbarum* polysaccharides from *Lycii Fructus* reduces endogenous ROS production and DNA damage (Hsieh et al., 2018). It also activates the immune system response, increases the expression of IL-6 and IL-1β in the serum and regulates gut microbiota to mitigate radiation damage (Zheng et al., 2021). Another study demonstrated that an aqueous extract of *Lycii Fructus* reduced oxidative stress and inflammation in mouse neurons (Guo et al., 2021).

Moreover, tonic herbs such as *Ophiopogonis Radix*, *Atractylodis Macrocephalae Rhizoma* (Baizhu in Chinese), *Acanthopanacis Senticosi Radix* et *Rhizoma* seu *Caulis* and others have been shown to have some therapeutic effects on RI. They inhibit oxidative stress and improve the inflammatory state. *Acanthopanacis Senticosi Radix* et *Rhizoma* seu *Caulis* shows better effect on the prevention and treatment of radiological brain damage (Zhou et al., 2018b).

4.1.3. TCM for promoting blood circulation and resolving stasis

According to the theory of TCM, the class of TCMs that invigorate blood circulation and eliminate blood stasis are used to treat

Table 1
Anti-radiation effects and mechanisms of action of various TCMs.

Category	TCM	Active ingredient	Drug delivery model	Mode of administration	Doses	Administration times	Anti-radiation mechanisms	Impacts	References
Clearing heat and removing toxins	*Polygoni Cuspidati Rhizoma* et *Radix* (Huzhang)	Polydatin	Male Balb/c mice	Intraperitoneal injection	100 mg/kg	30 d	Regulation of *HO-1* pathway, inhibition of apoptosis	Restoration of haematopoietic system function	Guo et al., 2020
	Polygoni Cuspidati Rhizoma et *Radix* (Huzhang)	Polydatin	Male mice	Intraperitoneal injection	50, 100 mg/kg	6 d	Inhibition of the PI3K/AKT/mTOR pathway	Improvement of pulmonary fibrosis	Chen et al., 2023
	Scutellariae Radix (Huangqin)	Baicalin	SPF grade female C57BL/6 mice	Intraperitoneally injected	50, 100, and 200 mg/kg	16 weeks	Reduced TGF-β, TNF-α, IL-6 and IL-1β levels and inhibited Cyslts/Cyslt1	Prevention of radiological lung injury	Bao et al., 2022
	Rhei Radix et *Rhizoma* (Dahuang)	Rheum tanguticum polysaccharide	Male adult SD rats	Administered orally	100 mg/mL	7 d	Nrf2/*HO-1* pathway	Improvement of radiation bowel injury	Zhang, et al., 2020c;
	Scutellariae Radix (Huangqin)	Baicalin	Male Swiss mice	Administered orally	50 mg/kg	4 d	Reduces ROS and affects NF-κB pathway	Anti-inflammatory	Kumar Maurya & Lomte, 2022
	Glycyrrhizae Radix et *Rhizoma* (Gancao)	Glycyrrhetinic Acid	Female C57BL/6 mice	Gavage	40 mg/kg	–	Inhibition of TGF-β1 secreted by Treg cells induces EMT and MFB transformation	Alleviation of radiological pulmonary fibrosis	Chen et al., 2024b
	Glycyrrhizae Radix et *Rhizoma* (Gancao)	Glycyrrhizin	Male C57BL/6 mice	Intraperitoneally injected	5, 10, and 20 mg/kg	3 d	TNF-α, IL-1β and IL-6, HMGB1/TLR4 pathway	Mitigation of acute radiological lung injury	Zhang et al., 2020e; Zheng et al., 2020
	Andrographis Herba (Chuanxinlian)	Andrographolide	Female C57BL/6 mice	Intraperitoneal injection	5, 10, and 20 mg/kg	4 weeks (every other day)	Inhibition of AIM2 inflammasome-mediated pyroptosis	Improvement of radiological lung injury	Gao et al., 2019
	Andrographis Herba (Chuanxinlian)	Andrographolide	Female Swiss albino mice	Topical application	3.6 mg/kg	10 d	Reduction of inflammatory protein expression, prevention of *p53* overexpression	Protecting the skin from damage	Indirapriyadarshini, Kanimozhi, Natarajan, & Jeevakaruniyam, 2023
Tonic category	*Astragali Radix* (Huangqi)	Astragalus decoction	SPF grade male Balb/c mice	Gavage	3 g/mL	14 d	Prevents reduction of white blood cells, red blood cells, haemoglobin, protects spleen, thymus gland	Prevention of acute radiation damage	Wei, Cheng, Wang, & Du, 2023
	Astragali Radix (Huangqi)	Radix astragali polysaccharide	Mesenchymal stem cell MSC	Collaborative programme	50 μg/mL	3 d	Bcl-2, Bcl-xl, Bax and Bak, mitochondrial pathway	Prevention of radiation-induced bystander effects	Zhang, et al., 2020f
	Astragali Radix (Huangqi)	Astragaloside IV	Male wild-type C57BL/6 mice, Sprague Dawley rats	Intraperitoneal injection	20, 40 mg/kg	30 d	BDNF/trkb pathway, inhibition of cellular iron death	Radiological lung injury	Liu et al., 2023b; Chen & Wu, 2023
	Ophiopogonis Radix (Maidong)	Ophiopogonin C	Male inbred C57BL/6 mice	Gavage	3 mg/kg	4 weeks	Enhanced SOD activity, inhibition of oxidative stress	Prevention of radiological pulmonary fibrosis	Fu, Li, & Yao, 2022
	Ophiopogonis Radix (Maidong)	Ophiopogonis Radix	Male C57BL/6 mice	Gavage	1.85 mg/mL	14 d	Inhibition of IL-6, TNF-α and TGF-β1, hydroxyproline, MDA, MMP-2 and TIMP-2	Reduction of radiation lung inflammation	Yao, Wang, Li, & Zhang, 2019
	Lycii Fructus (Gouqizi)	*Lycium barbarum* extract	ARPE-19	Pretreated with *L-Barbarum* extracts	0–200 μg/mL	2 h	Reduces ROS and DNA damage	Reduces UVB-induced cellular damage	Hsieh et al., 2018
	Lycii Fructus (Gouqizi)	*Lycium barbarum* extract	Male C57BL/6 mice	Oral administration	1.0, 3.0, and 9.0 g/kg	28 d	Regulates immunity, regulates intestinal flora	Improvement of radiation-induced intestinal damage	Zheng et al., 2021
	Lycii Fructus (Gouqizi)	*Lycium barbarum* extract	Male SPF BALB/c mice	Pretreated with LBP	10 g/kg	4 weeks	Reduces oxidative stress, inhibits neuroinflammation	Prevention of radiation-induced cognitive	Guo et al., 2021

(*continued on next page*)

Table 1 (*continued*)

Category	TCM	Active ingredient	Drug delivery model	Mode of administration	Doses	Administration times	Anti-radiation mechanisms	Impacts	References
								impairment	
	Lycii Fructus (Gouqizi)	*Lycium barbarum* polysaccharide-glycoprotein	Human keratinocyte hacat cells	Collaborative programme	0.1–1.5 mg/mL	–	Activation of Nrf2, reduction of oxidative stress, inhibition of iron death	Prevention of radiation-induced oral mucositis	Jiang et al., 2023
	Ginseng Radix et *Rhizoma* (Renshen)	Crude extract of ginseng	C57BL /6J mice	Gavage	200 mg/kg	–	*P53*-PUMA, apoptosis, reduction of DNA damage	Intestinal radiation injury	Zhang et al., 2023
	Acanthopanacis Senticosi Radix et *Rhizoma* seu *Caulis* (Ciwujia)	Acanthopanax Extract	Male *Kun-Ming* mice	Oral administration	235.7 mg/kg	14 d	SOD, CAT, MDA and GSH, inhibits oxidative stress, and protects neuronal cells	Radiation brain damage	Song et al., 2022; Zhou et al., 2018a; Zhou et al., 2018b
	Atractylodis Macrocephalae Rhizoma (Baizhu)	Atractylenolide II	Hacat cells	Collaborative programme	50 μmol/L	1, 3 or 5 d	Regulation of the mapkp38/Nrf2 pathway	Mitigation of radiation damage	Xiao et al., 2020
	Ganoderma (Lingzhi)	Ganoderma lucidum extract	Male Swiss albino mice	Oral administration	400, 800 mg/kg	15 d	Reduces lipid peroxidation and lowers Il-2, TNF-α, IF-γ levels	Reduction of the inflammatory response	Bala et al., 2022
	Rhodiolae Crenulatae Radix et *Rhizoma* (Hongjingtian)	Rhodioloside	Wistar rat	Intraperitoneal injection	100 mg/kg	7 d	Reduced ROS production, mitochondrial oxidative stress	Prevention of salivary gland damage	Sun et al., 2022
	Amomi Fructus (Sharen)	Amomi Fructus	C57BL/6 mice	Oral administration	250 mg/kg	10 d	Enhanced expression of Nrf2 and its target genes regulates antioxidant responses	Suppression of radiation-induced inflammatory responses	Drishya, Dhanisha, Raghukumar, & Guruvayoorappan, 2022
Promoting blood circulation and eliminating blood stasis	*Curcumae Longae Rhizoma* (Jianghuang)	Curcumin	SD rats	Gavage	30 mg/kg	14 d	Inhibition of TNF-α, IL-1β and IL-6, regulation of NF-κB pathway	Prevention of radioactive liver injury	Li, Jiang, Lu, Liu, & Ling, 2021
	Croci Stigma (Xihonghua)	Saffronin	Rat intestinal epithelial IEC-6 cells	Collaborative programme	0.1, 1, 10, and 100 μmol/L	24 h	TNF-α, IL-1β and IFN-γ, increased SOD, CAT and gpx activities	Protection of intestinal epithelial cells	Zhang et al., 2020a
	Croci Stigma (Xihonghua)	Saffronin	Male Wister albino rats	Intraperitoneal injection	50 mg/kg	7 d	Oxidative stress, inflammation, FOXO/AKT pathway	Prevention of radiation damage	El-Sheikh, Aziz, Abdelrahman, & Mohmad, 2023
	Salviae Miltiorrhizae Radix et *Rhizoma* (Danshen)	Cryptotanshinone	Male Sprague-Dawley rats	Oral administration	20 mg/kg	5 d	IL-6 and IL-10, TGF-β1, NOX-4 and MMP-1, inhibition of CCL3/CCR1	Relief of lung injury and fibrosis	Jiang et al., 2019
	Salviae Miltiorrhizae Radix et *Rhizoma* (Danshen)	Tanshinone IIA	H9c2 cell	Collaborative program	10 μg/mL	48 h	Regulation of *p38*/*p53* pathway	Prevention of cardiomyocyte damage	Wang et al., 2022b
	Radix Scopoliae (Shanlangdang)	Anisodamine	Male C57BL/6 mice	Intraperitoneal injection	5 mg/kg	6 weeks (every other day)	Reduction of DNA damage, activation of Nrf2/ARE pathway, enhancement of antioxidant capacity	Mitigation of radiological lung injury	Guo et al., 2023

Table 2
TCM prescriptions for the treatment of radiation injury.

Formulation	Name	Efficacy	Forms	Doses	Administration time	Functions	References
Decoction	Huangqi Decoction	Yiqi Gubiao	*Astragali Radix* (Huangqi), *Rehmanniae,* etc.	4.5, 9, and 18 g/(kg·d)	14 d	NF-κB pathway, inhibition of apoptosis and inflammation	An et al., 2021
	Huangqi Decoction	Yiqi Gubiao	*Astragali Radix, Rehmanniae,* etc.	4.5, 9, and 18 g/(kg·d)	7 d	TLR4/myd88/NF-κB pathway, treatment of hypothalamic injury	Jiang et al., 2023
	Guiqi Baizhu Decoction	Removing fire and detoxifying toxins	*Astragali Radix, Atractylodis Macrocephalae Rhizoma* (Baizhu) etc.	4.1, 8.2, and 16.4 g/kg	7 d	Regulation of intestinal flora NF-κB pathway, improves radiation inflammation	Zhang et al., 2020b; Li et al., 2021b
	Guiqi Baizhu Decoction	Removing fire and detoxifying toxins	*Astragali Radix, Atractylodis Macrocephalae Rhizoma* etc.	0.41, 0.82, and 1.64 g/mL	7 d	Ameliorates oxidative stress AQP4 and Na^+/K^+-atpase	Li, et al., 2022b
	Danggui Buxue Tang (DBT)	Tonifying the vital energy and nourishing the blood	*Astragali Radix, Angelicae Sinensis Radix* (Danggui)	10 μL/g, 12 g/kg	8 weeks	Nrf2/HMGB1 pathway, protects against radiological heart injury	Huang et al., 2022
	Yiqi Jiedu Tang	Clearing heat and removing toxins	*Astragali Radix,* etc.	33.14 g/kg	10 d	TLR5 pathway, attenuating testicular injury in mice	Wang et al., 2020a
	Yiqi Jiedu Tang	Clearing heat and removing toxins	*Astragali Radix,* etc.	0.2 mL of 5.8, 11.6, and 23.2 g/kg/day	5 d	Promotes DNA repair, NF-κB pathway, protects spermatocytes	Zhang et al., 2022b
	Yiqi Jiedu Tang	Clearing heat and removing toxins	*Astragali Radix,* etc.	5.8 g/kg/day	5 d	IκBα/NF-κB pathway, inhibition of spermatocyte autophagy and apoptosis	Zhang et al., 2024
	Yiqi Jiedu Tang	Clearing heat and removing toxins	*Astragali Radix,* etc.	16.57 and 33.14 mg/g	10 d	Regulate immunity and inhibit apoptosis	Wang et al., 2022a
Ointment	Shayu Paste	Clear heat and cool blood	*Sanguisorbae Radix* (Diyu)	–	29 d	Inhibits apoptosis and promotes repair of skin damage	Wang et al., 2019
	Huanglian Jiedu plaster (HJP)	Clearing heat and removing toxins	*Coptidis Rhizoma* (Huanglian), etc.	–	15 d	Regulates HMGB1, improves radiodermatitis	Wang et al., 2023b
	Huanglian ointment	Clearing heat and removing toxins	*Coptidis Rhizoma*	–	7 d	Improves skin inflammation and reduces infection	Li, Gao, Song, Zhang, & Li, 2023
	Moist exposed burn ointment (MEBO)	Clearing heat and removing toxins	*Phellodendri Chinensis Cortex* (Huangbo), etc	–	Twice a day	Prevention of radioactive skin damage	Gao & Wu, 2019
	Huangqin ointment	Clear heat and dampness	*Scutellariae Radix*	–	Twice a day	Improvement of radioactive skin damage	Wang, Zang, Qin, Di, & Qiu, 2021

radiation-induced blood heat and blood stasis syndromes, invigorate blood circulation and regulate yin and yang. For example, *Curcumae Longae Rhizoma* is a typical TCM that activates blood circulation and removes blood stasis, with the effect of breaking down *qi* and promoting blood circulation, and relieving menstruation and pain. The study has discovered that curcumin has a favorable effect on inflammation (Zhang et al., 2022a). It has been shown to increase the activity of antioxidant enzymes, modulate the NF-κB pathway, inhibit oxidative stress and ameliorate inflammatory responses (Li, Jiang, Lu, Liu, & Ling, 2021; Shabeeb, Musa, Abd Ali, & Najafi, 2020). *Salviae Miltiorrhizae Radix* et *Rhizoma* has the effects of activating blood circulation, removing blood stasis, promoting menstruation and relieving pain (Zhan et al., 2023). Cryptotanshinone is one of its major active ingredients, which possesses various pharmacological activities such as anti-inflammatory, anti-immune modulation and anti-fibrosis (Li et al., 2021a). It was found to be resistant to radiation damage to cardiomyocytes, which may be related to its ability to reduce oxidative stress and regulate the *p38*/*p53* pathway (Wang et al., 2022b). Notably, it has been pointed out that tanshinone IIA can inhibit the abnormal increase of fibroblasts, and the self-soluble microneedles made of it can effectively inhibit the proliferation of human skin fibroblasts (Zhan et al., 2023). But tanshinone IIA has not been studied in radiation-induced dermal fibrosis. In addition, it was shown that cryptotanshinone ameliorates dysregulation of gut microbiota and bile acid metabolism in mice with radiation-induced pulmonary fibrosis (Li et al., 2023c).

In addition to those mentioned above, the therapeutic effects of RI or the anti-radiation potential of many other types of TCM have been demonstrated. For example, *Croci Stigma, Andrographis Herba* (Chuanxinlian in Chinese) and *Rhei Radix* et *Rhizoma* (Dahuang in Chinese), etc. *Ganoderma* and *Saussurea involucrata* polysaccharide can mitigate irradiation-induced oxidative damage (Bala et al., 2022; Yu, Fu, Guo, Lian, & Yu, 2020). Besides, *S. involucrata* polysaccharide reduce DNA damage (Guo et al., 2024; Wang et al., 2023c).

4.2. TCM prescriptions

4.2.1. Decoction

TCM decoction is the most commonly used traditional dosage form. It is able to synthesize the therapeutic effects of various medicines and treat diseases in a comprehensive manner. The research shows that Huangqi decoction could decline the secretion of spleen inflammatory factors IL-1β and IL-6, thus repairing the blood-forming system, immune system and kidney damage caused by radiation (Yan et al., 2021b). In further researches, it was found to prohibit apoptosis by regulating the NF-κB pathway and regulating the expression of B-cell lymphoma 2 (Bcl-2)/pro-apoptotic proteins (Bax) and Caspase-3 (An et al., 2021; Yan et al., 2021a). In a research study, moreover, it has been demonstrated that Guiqi Baizhu Decoction can alleviate radiation-induced inflammatory responses by regulating the gut microbiota (Zhang et al., 2020b). It also improves hypoxia problems and excessive oxidative stress, regulates the expression of Aquaporin 4 (AQP4) and Na^+/K^+-ATPase, and provides therapeutic protection against radiation-induced intestinal oedema (Li et al., 2022b).

Yiqi Jiedu Decoction (YQJD) can clear heat and detoxify toxins, benefit *qi* and nourish *yin*, and is a TCM decoction that has been proven to have radiation protection effects (Wang et al., 2020a; Zhang et al., 2022b). Research has shown that YQJD Tang increases testicular index and improves spermatogenic tubule structure, and inhibits the expression of inflammatory proteins IL-6 and IL-1β by promoting DNA damage repair (Wang et al., 2020a; Wang, Zhang, & Yang, 2021; Zhang et al., 2022b). Furthermore, radiation-induced autophagy and apoptosis in spermatocytes were inhibited by inhibiting the phosphorylation of inhibitor of nuclear factor kappa B α (IκBα)/NF-κB pathway-related factors and regulating the expression of Beclin-1 and Bcl-2 proteins (Zhang et al., 2024). In addition, it was found that Danggui Buxue Tang (DBT) has good therapeutic effects on radiation-induced myocardial damage (Huang et al., 2022).

4.2.2. Ointment

Ointment is a commonly used herbal topical preparation, which is mainly inclined to the study of the treatment of radiation-induced skin damage. For example, Shayu Paste has been found to regulate Bax/Bcl-2 balance to inhibit apoptosis and promote healing of skin injuries (Wang et al., 2019). Huanglian Jiedu plaster (HJP), which has the effect of clearing heat and removing toxins, has a good therapeutic effect on inflammation and so on. It was found to inhibit the expression of HMGB1 *in vivo* and *in vitro*, and to be effective in ameliorating radiation skin inflammation (Wang et al., 2023a). Li et al. pointed out that the self-made Huanglian ointment of the hospital for radioactive skin lesions significantly reduced pain after 12 h of treatment, and wounds were essentially healed after 2–3 d of treatment (Li, Gao, Song, Zhang, & Li, 2023). As well, moist exposed burn ointment (Gao & Wu, 2019) and Huangqin Ointment (Wang, Zang, Qin, Di, & Qiu, 2021) have demonstrated good therapeutic effects in clinical practice for the treatment of different degrees of radioactive skin injuries. However, most of these preparations have not elucidated the specific mechanisms for the treatment of radioactive skin injuries.

In summary, TCM has enormous research value and development prospects in the treatment of radiation injury. Currently, there are more basic studies on TCM in the area of anti-radiation. However, although clinical studies can further confirm the efficacy of TCM in preventing and treating RI, the scale of reported clinical studies so far is limited. According to the literature, Chinese herbal medicines such as *Ophiopogonis Radix*, *Glycyrrhizae Radix* et *Rhizome*, and *Rehmanniae Radix* (Shengdihuang in Chinese) are commonly used in the clinical treatment of radioactive lung injury (Zhang et al., 2023). For radioactive skin injuries, Chinese herbal medicines such as *Arnebiae Radix* (Zicao in Chinese), *Phellodendri Chinensis Cortex* (Huangbo in Chinese) and *Coptidis Rhizoma* (Huanglian in Chinese) are commonly used (Chen et al., 2024a). However, most of these Chinese medicines still lack in-depth research on the pharmacological substance basis and mechanism of action, which cannot be widely applied in clinical practice at present. Therefore, in order to achieve the transformation and application of TCM preparations in clinical practice, it is necessary to fully utilize modern scientific technology to deeply explore the active ingredients and mechanism of anti-radiation of TCM, and actively carry out preclinical research to provide sufficient data support for clinical trials.

5. Application of new TCM preparations for anti-RI

In the treatment of RI, there are also some relatively new types of Chinese medicinal dosage forms such as nanoparticles and microspheres for targeted therapy, as well as topical sprays and gels, etc. Currently, new dosage forms of TCM in anti-RI are mainly studied in nanoparticles, microspheres, films, gels, injections and sprays etc. (Fig. 3; Table 3).

5.1. Nanoparticles

Nanotechnology has been widely researched in TCM, which can overcome the problems of poor water solubility and stability of certain TCMs, and at the same time realize targeted therapy and improve the bioavailability (Wei et al., 2022). For example, curcumin from the *Curcumae Longae Rhizoma* has poor water solubil-

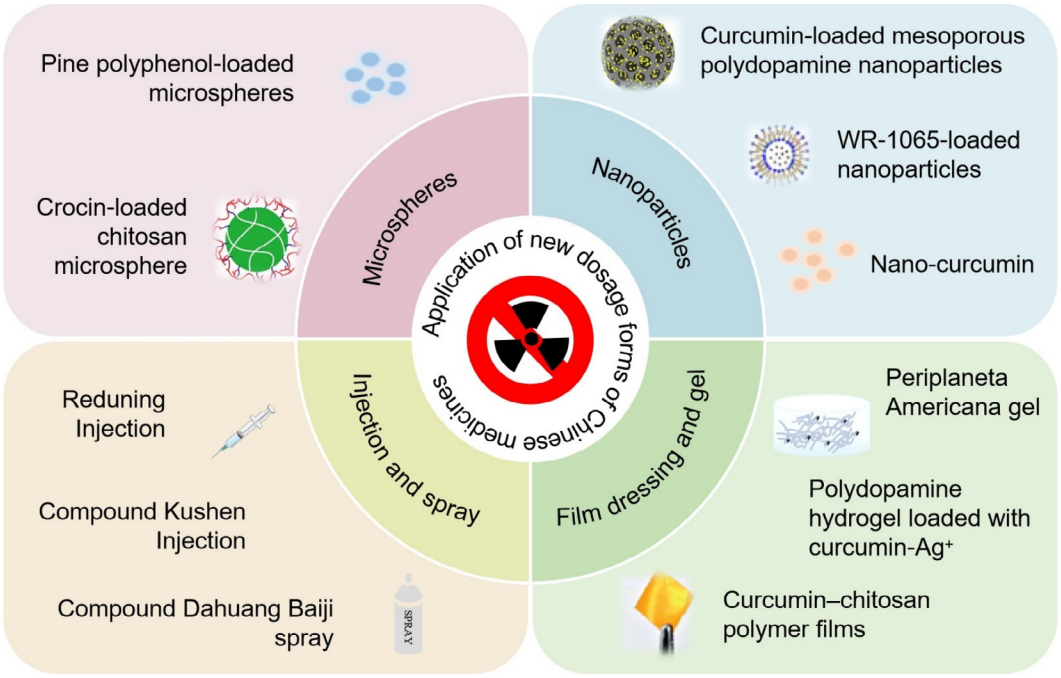

Fig. 3. Novel preparations of TCM in radiation injury.

Table 3
Application of new TCM preparations for anti-RI.

Names of dosage form	Advantages/disadvantages	Names of preparation	Formula	Effects or functions	References
Nanoparticles	Improving drug solubility and bioavailability, and enabling targeted therapies	Curcumin nanomedicines	Curcumin	Reducing radioactive intestinal damage	Ghanbarzadeh et al., 2023
		Curcumin-loaded mesoporous polydopamine nanoparticles	Curcumin, mesoporous polydopamine nanoparticles	High drug loading capacity, improvement of radioactive lung inflammation	Chen et al., 2022
		WR-1065-loaded nanoparticles	Curcumin, Thioketal to poly (ethylene glycol)–poly (ε-caprolactone) polymer, WR-1065 (the active ingredient of amifostine)	ROS-sensitive, prevention and treatment of RI	Liu et al., 2021
Microspheres	Improving bioavailability, and protecting medications and masking bad scents, and controlled release of drugs	Crocin-loaded chitosan microspheres	Crocin, chitosan	ROS-sensitive, lung targeting, improvement of radiation lung injury	Wang et al., 2023b
		Pine polyphenol-loaded microspheres	Pinecones of *P. koraiensis* chitosan	Improving the absorption efficiency and utilization rate of polyphenols *in vivo*.	Yi et al., 2018
Films	Prevention and treatment of RI, skin injuries	Curcumin–chitosan polymer films	Crocin, chitosan	Radiation-sensitive, amount of drug released	Chauhan et al., 2020
Injections	Fast-acting treatment, unpredictable side effects of treatment	Reduning Injection	*Lonicera japonica* Thunb, *Gardenia jasminoides* Ellis, and *Artemisia annua* L.	Multiple targets of action, improving radiation-induced inflammation and pulmonary fibrosis	Yang et al., 2022
		Compound Kushen Injection	*Sophora flavescens* Ait. (Kushen), *Heterosmilax yunnanensis* Gagnep. (Baituling)	Remarkable therapeutic effects	Liu et al., 2023a
Sprays	Radioactive skin damage	Compound Dahuang Baiji spray	*Rhei Radix* et *Rhizome* (Dahuang), *Bletillae Rhizoma* (Baiji)	Regulating ALOX5 and inhibits inflammation	Wen et al., 2023
Gels	Controlling release of drugs, and improving bioavailability	Polydopamine hydrogel loaded with curcumin-Ag^+	Curcumin, polydopamine, 4-arm-polyethylene glycol	Prevention of radiation damage	Su et al., 2024
		Periplaneta Americana gel	*Periplaneta Americana*, poloxamer, ethanol, glycerin	Improvement of radioactive skin inflammation	Que et al., 2023

ity, instability and low bioavailability, and is therefore very limited in clinic use (Chen et al., 2022). It was demonstrated that curcumin nanomedicines were able to achieve targeted treatment of radiation damage with significantly increased bioavailability (Ghanbarzadeh et al., 2023). Chen et al. prepared a curcumin-loaded mesoporous polydopamine nanoparticles. It could directly

target curcumin to lung tissues by inhalation administration, which significantly improved the therapeutic effect of curcumin on radiation pneumonitis (Chen et al., 2022). In addition, Liu et al. developed a novel ROS-sensitive oral delivery system of curcumin and amphotericin (WR-1065-loaded nanoparticles). It could avoid the adverse effects associated with intravenous amphotericin and also enable the release of the drugs after exposure to radiation, which together achieve the radiation protection effect (Liu et al., 2021).

Besides, it has been pointed out that self-assembled aggregates are commonly found in the decoction of TCM, which can not only exert biological activities, but can also be used as natural carriers for drug delivery (Meng et al.). This can obviously improve the efficacy of the medication. This novel herbal self-assembled nanoparticle may have good potential for the treatment of RI.

5.2. Microspheres

Microspheres are newly developed drug delivery vehicles for targeted drug delivery systems. It provides drug protection and controlled drug release, as well as high biocompatibility (Yawalkar, Pawar, & Vavia, 2022). For example, Wang et al. prepared a kind of ROS-sensitive Crocin-loaded chitosan microspheres, and found that the microspheres of about 10 μm had good passive targeting to the lungs and the retention time was more than 48 h. This enhanced the antioxidant activity of Crocin, which significantly enhanced the antioxidant enzyme activities and inhibited the release of inflammatory factors in mice (Wang et al., 2023b). These results indicated that Crocin microspheres are highly effective in radiological protection against radiation lung injury. In another research, novel chitosan-loaded microspheres from the pine cones of red pines (Haisongzi in Chinese) improved the absorption efficiency and utilization rate of polyphenols *in vivo*, which reduced radiation-induced oxidative stress (Yi et al., 2018). Microspheres can mask the bad smell of drugs while improving bioavailability, and could effectively improve patient compliance. But the research on TCM microspheres in terms of RI is still relatively scarce.

It has been pointed out that the use of some radiation-responsive natural macromolecules (e.g., polysaccharides) as carrier materials for drugs can achieve both smart, targeted release and improved drug bioavailability (Zheng, Zhu, Guo, & Zhang, 2023). Therefore, the use of some radiation-responsive materials as carrier backbones for radiation-resistant TCM microspheres may be surprisingly effective in preventing RI.

5.3. Films

Film is a new type of wound dressing. The film drug delivery system enables precise and slow controlled release drug delivery with the advantages of stable drug delivery, maintenance of local mucosal and plasma drug concentration, greatly improved drug utilisation and fewer side effects (Li et al., 2022a). Rajat Chauhan et al. prepared a curcumin-chitosan film, which is a novel radiation-responsive drug delivery system. The release of curcumin increased significantly under radiation exposure at a dose of 2 Gy, while the release of curcumin was complete at 6 Gy (Chauhan et al., 2020). The use of TCM films in clinical practice has become more widespread, but there is still little research on radiation damage.

5.4. Other new preparations

In addition to the new preparations mentioned above, there are also Chinese medicine injection nights, sprays and gels. For instance Reduning Injection (Yang et al., 2022) and Compound Kushen Injection (Liu et al., 2023a) are both more effective in treating RI. However, due to the complexity of the components of herbal medicines, its injections have been less studied because of the unpredictable side effects it brings. Research shows that the TCM Compound Dahuang Baiji spray can regulate arachidonate 5-lipoxygenase (ALOX5) expression and improve radioactive skin inflammation (Xu et al., 2023). In addition, Su et al. prepared a polydopamine hydrogel loaded with curcumin-Ag^{+}, which was found to be effective in reducing radiotherapy-induced cellular radiation damage (Su et al., 2024). It has been noted that *Periplaneta Americana* gel used in clinical therapy effectively relieves acute radiation dermatitis and reduces the incidence of chronic radiation skin inflammation (Que et al., 2023). It is notable that Xiang et al. developed a radiation-responsive wearable microneedle drug delivery system for the prevention of RI (Yu et al., 2022), but there are no relevant studies in TCM at the moment.

The research of these new dosage forms overcomes the shortcomings of TCM in clinical application. For example, the problems of difficult solubility and poor bioavailability of certain TCM ingredients have been improved. At the same time, compared with TCM preparations, the new dosage form has a faster effect as well as enables multiple routes of administration and improves patient compliance. In addition, new dosage forms of TCM can not only promote the innovative development of TCM in anti-radiation injury, but also contribute to the clinical treatment of radiological RI in TCM with important significance.

6. Conclusion and perspectives

As mentioned above, TCM plays an important role in the treatment of RI and has demonstrated unlimited potential in anti-RI. Radiation poisons attack the body, disrupting its balance and causing an imbalance between *yin* and *yang*. The efficacy of TCM in clearing heat and removing toxins, benefiting *qi* and tonifying *yin*, and activating blood circulation and removing blood stasis is a key factor in reversing these problems (Gu et al., 2020; Yang, Li, Yang, & Wu 2021). Modern research further indicates that TCM has demonstrated anti-RI capacity in suppressing oxidative stress, anti-inflammation and regulating immunity. More importantly, TCM has fewer adverse effects compared to chemical drugs, and its price makes it more accessible to most patients compared with cell therapy and gene therapy. In short, the above unique advantages provide enormous scope for the development of TCM in the therapy of RI. In the future, it is necessary to further strengthen the research and development of TCM against RI to promote its clinical application and promotion.

Although TCM has been widely used in the clinic for the treatment of RI, most of them still lack relevant material basis and mechanism research (Zhou et al., 2023). Therefore, further research is needed on the material basis and mechanism of action of Chinese herbal medicine anti-RI. Modern pharmacological research has shown that ferroptosis, macrophage polarization, and regulation of gut microbiota play important roles in the anti-RI (Guo et al., 2022; Yi, Lu, Shen, Wu, & Zhang, 2023; Zhang et al., 2020d). Based on the above relevant mechanisms, further in-depth exploration of the material basis and mechanism of action of TCM in treating RI will be a key and difficult issue to focus on at present. With the development of modern science and technology and artificial intelligence, network pharmacology and molecular docking technology can be applied to screen and verify effective substances and targets of TCM for anti-RI (Li et al., 2023b). Simultaneously, proteomics technology can be used to analyze the dynamically changing protein composition and activity patterns in cells from a holistic perspective to reveal potential target proteins or protein biomarkers, which coincides with the "holistic

view" and "dynamic view" of TCM (Yuan et al., 2020). Therefore, the application of these techniques mentioned above can be beneficial in revealing the potential material basis and mechanism of TCM for anti-RI and facilitate the development of new drugs.

As is well known, TCM formulations are greatly limited in their clinical efficacy due to their complex active ingredients and poor absorption caused by insoluble substances. Therefore, there is an urgent need to develop new dosage forms and delivery systems of TCM for anti-RI. More interestingly, the combination of TCM and Western medicine provides the possibility for designing new and efficient dosage forms and delivery systems for the treatment of RI. For example, combining TCM with chemical drugs to make a targeted drug delivery system, etc., which can achieve increased effectiveness and reduced toxicity (Liu et al., 2021). Due to the presence of a ROS rich microenvironment in the RI site, a novel ROS-responsive drug delivery system can be designed to achieve targeted drug release and efficient treatment of RI. In addition, new preparations such as self-assembled nanoparticles, multilayer drug loaded water gel and microneedles can exert synergistic effects in a variety of TCM. Among them, due to the painless and non-invasive ability of microneedles to break through the skin barrier and improve drug transdermal efficiency (Lim & Kim, 2022), microneedles therapy is most suitable for percutaneous treatment of skin injury caused by radiation. Therefore, the design of new formulations can solve the clinical application limitations of TCM preparations for anti-RI, which will further promote the clinical application of anti-radiation TCM. Obviously, TCM has certain advantages in preventing and treating RI and has a wide range of application prospects. Through continuous in-depth research and development, TCM radiation protection drugs with high efficiency, low toxicity, and both prevention and treatment will be of great significance for the clinical treatment of RI.

CRediT authorship contribution statement

Lixue He: Conceptualization, Writing – review & editing, Visualization. **Shixing Edi:** Writing – review & editing. **Jun Ma:** Writing – review & editing. **Zilin Kong:** Writing – review & editing. **Chunguang Dai:** Writing – review & editing. **Linfang Huang:** Writing – review & editing. **Rui Zeng:** Resources, Supervision, Funding acquisition, Writing – review & editing. **Kaijun Gou:** Conceptualization, Resources, Supervision, Writing – review & editing.

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.

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