REVIEW

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Notoginsenoside R1: a systematic review of its pharmacological properties

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Notoginsenoside R1 is one of major bioactive compounds extracted from *Panax notoginseng* (Burk.) dry roots and rhizomes of F.H.Chen, which has been increasingly used for enhancing cognition and physical health worldwide. The objective of this study was to review the pharmacological effects of notoginsenoside R1 in a systematic manner. We performed searches on databases including MEDLINE (Pubmed), Google Scholar and Web of Science, the System for Information on to select the original research publications reporting the biological and pharmacological effects of notoginsenoside R1 from *in vitro* and *in vivo* studies regardless of publication language and study design. Notoginsenoside R1 exhibited potent characteristics of neuroprotective, anti-inflammatory, anti-apoptosis and anti-ischemia-reperfusion injury properties etc. The cytotoxic effects of notoginsenoside R1 were dependent on different types of cell lines. Other pharmacological effects including accumulation of lipopolysac chaired-induced microcirculation, endothelial injury, hypoxia-reoxygenation injury effects have been mentioned, but the results were considerably diverged. A higher quality of evidence on clinical trial studies is highly recommended to confirm the efficacy of notoginsenoside R1.

1. Introduction

For many years, notoginseng has been used as a nutritional supplement for the body and a tonic for prolonging life. It has increasingly achieved more popularity to become one of the most consumed herbal nutritional products. Especially, notoginsenoside R1 (Fig. 1), a novel phytoesteogen, was isolated from *Panax notoginseng* (Zhou et al. 2017; Tian et al. 2018). It has found that the pharmacological properties of *Panax notoginseng* are mainly attributed to the effect of notoginsenoside R1 (Chen et al. 2016). In addition, it has been reported that the compound can effectively stimulate the central nervous system and promote mental acuity and intelligence (Zhang et al. 1997a; Xiong et al. 2017). It was shown that notoginsenoside R1 plays an active role in the protection of the nervous system, inhibits the growth of tumors and assists the treatment of dexa-methasone in chronic inflammatory diseases (Ji et al. 2017; Yang et al. 2017a). It has been reported that notoginsenoside R1 inhibits human colorectal cancer metastasis (Pang et al. 2017). Notoginsenoside R1 could alleviate chronic hypoxic pulmonary hypertension in mice (Wang et al. 2016a; Chen et al. 2017a) and exhibited immune stimulation effects (Zhang et al. 2016). In summary, current research has proven the important role of this compound. Nonetheless, there is no critically evaluated review of the pharmacological effects of notoginsennoside R1 based on summarizing the current reliable evidence. Therefore, the purpose of our study was to systematically review the pharmacological actions of notoginsennoside R1 in the published literature.

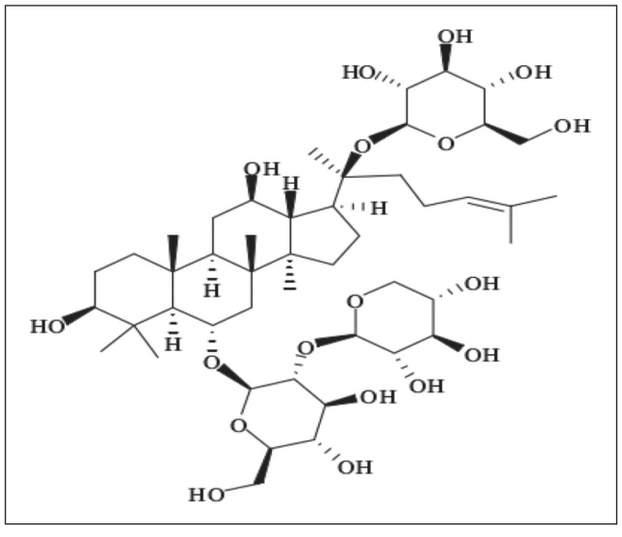

Fig. 1: Chemical structure of notoginsenoside R 1.

2. Traditional use of *Panax notoginseng*

Panax notoginseng (Araliaceae), commonly known as Sanqi (Si et al. 2016; Wang et al 2107b), is a traditional herbal Chinese medicine (He et al. 2015; Yang et al. 2016a). It has been widely used in oriental countries for thousands of years (Wei et al. 2015; Fan et al. 2016). Now, *Panax notoginseng* is a popular natural medicine traditionally used for its hemostatic (Ren et al. 2015) and restorative properties (Xia et al. 2016; Huang et al. 2017a). In addition, it seems to have positive effects on blood circulation, blood stasis removal and pain relief (Wenxi et al. 2015; Wei et al. 201) and had been widely used to prevent and treat microcirculation disorders (Pan et al. 2015; Wu et al. 2016). Plenty of pharmacological properties have been reported on *Panax notoginseng* (Cai et al. 2016; Luo et al. 2019). It shows that *Panax notoginseng* can reduce inflammatory reactions in patients and animal models (Hu et al. 2015; Zhou et al 2019) and ameliorate the symptoms of experimentally disseminated intravascular coagulation (Li et al2016; Shi et al. 2017). Based on the extensive pharmacological properties of Panax notoginseng, it provides an important basis for the research of notoginsenoside R1.

Table 1: Pharmacological actions of notogisengnoside R1 on the nervous system

Neurological disease	Research target	Mechanism
Alzheimer's disease	Amyloid-β-protein	Increased the membrane excitability of CA1 pyramidal neuronsin hippocampal (Yan et al. 2013)
		Inhibiting reactive oxygen species and modulating MAPK activation (Ma et al. 2014)
		Up-Regulating Insulin Degrading Enzyme and Inhibiting Aβ Accumulation (Li et al. 2015)
Cerebral ischemia disease	Estrogen-like effects	Accelerating the activa-tion of the ATF6 / Akt signaling pathway via estrogen receptors(Hou et al. 2017)
		Activating Nrf2/ARE signaling (Meng et al. 2014)
		Inhibition of NADPH oxidase activity and mitochondrial dysfunction via ER-dependent activation of Akt/Nrf2 pathways. (Meng et al. 2014b)
		Activation of endoplasmic reticulum stress pathways (Si et al. 2016)
Neuroprotective effect	NMDA receptor	Resistglutamate-induced intracellular ca $^{+}$ overload (Gu et al. 2009)
Promoted cortical neuron growth	Wnt/β-catenin signaling pathway	Treatment of β-catenin-knockdown neurons,β-catenin mRNA levels increased significantly(Tu et al. 2018).

3. Sources and bioavailability of notoginsenoside R1

The primary source of notoginsenoside R1 is *Panax notoginseng* plant material (Liu et al. 2015). It is found in higher concentrations in *Panax notoginseng* (around 2-4 %) roots than in *Panax ginseng* root (around 0.15-0.68 %) (Lelu et al. 2016). Stems and leaves of *Panax notoginseng* are generally containing lower concentrations of notoginsenoside R1 than the roots, rhizomes, or root hairs. *Panax notoginseng* saponins, including notoginsenoside R1, were isolated from root cultures o*f Panax notoginseng* (Liao et al. 2008). Notoginsenoside R1 is easily soluble in water (Liang et al. 2005), but ist apparent permeability was found to be very low in the single-layer Caco-2 cell permeability assay (Yu et al. 2013; Yang et al. 2017b). This result indicated that permeability is an important factor affecting the gastrointestinal absorption of notoginsenoside R1 following its oral administration (Guo et al. 2014; Xia et al. 2014). Fan et al (2018) found that the the oral bioavailability of notoginsenoside R1 and sodium has changed to some extent. Improvement of notoginsenoside R1 bioavailability made notoginsenoside R1 more and more reliable as a new type of drug in the future.

4. Pharmacological properties of notogisengside R1

The traditional medicinal use of *Panax notoginseng* had inspired many pharmacological investigations. It had been made in the search for new therapeutic agents, which led to numerous pharmacological studies on notoginsenoside R1.

4.1. Neuroprotective activity of notoginsenoside R1

Notoginsenoside R1 shows effects on patients with vascular dementia and cerebral ischemic stroke, and has therapeutic effects on chronic progressive neurodegenerative diseases such as Alzheimer's disease (Yan et al. 2013; Hou et al. 2017). Different principles of action have been proposed. Beta-amyloid protein (Aβ) accumulation could cause multiple neuronal damages and result in the cognitive impairments. Some studies found that notoginsenoside R1 could significantly decrease the amount of Aβ (Yang et al. 2016), it is thus a candidate for protecting the neuronal system and for treating Alzheimer's disease (Ma et al. 2014; Li et al. 2015). However, current research shows that notoginsenoside R1 only inhibits Aβ1-40, Aβ1-42 and Aβ25-35. The effect on Aβ's other types will be studied in the future.

Oxidative stress may also result the neurodegenerative diseases. Notoginsenoside R1 is regulating Akt and ERK1/2 pathways and Nrf2/ARE signal, so as to change phase II antioxidant enzymes (Meng et al. 2014a, b). The mechanisms of notoginsenoside R1 neuroprotection involves inhibition of NADPH oxidase activity and mitochondrial dysfunction *via* ER-dependent activation of Akt/Nrf2 pathways. Notoginsenoside R1 has a certain inhibitory effect on N-methyl-D-aspartate receptor (NMDAR)-mediated excitotoxicity, also a mechanism of neuroprotection (Gu et al. 2009). Notoginsenoside R1 has a positive effect on synaptic and memory dysfunction after amyloid protein elevation, thus promoting neuronal protection. By regulating the activation of reactive oxygen species and MAPK, notoginsenoside R1 can significantly alleviate amyloid-beta-induced neuronal damage. The results of notoginsenoside R1 research related to the nervous system were summarized in Table 1.

We conducted a literature review of the neuroprotective features of notoginsenoside R1, in traditional Chinese medicine for the treatment of various neurodegenerative diseases. The highlights are as follows: notoginsenoside R1 could mediate the restoration of inter-cellular communications within neurovascular units composed of neurons and other supporting cells that might be disturbed by an ischemic insult or traumatic injury. The present state of studies proved that notoginsenoside R1 is a useful and valuable resource of neuroprotective therapeutic agents.

4.2. Cardioprotective activity of notoginsenoside R1

The prevalence of cardiovascular diseases is a growing, and is even aggravated by the increase in the prevalence of diabetes. Hypertension, atherosclerosis and diabetic cardiomyopathy are major cardiovascular complications. Although current cardioprotective agents play a role in reducing cardiovascular-related complications, their efficacy is limited in protecting individual cardiovascular hearts. This has led to the screening of natural products with cardioprotective properties of great significance. Recent studies have shown that *Panax notoginseng* saponin R1 has strong antioxidant and anti-diabetic properties, which may help prevent cardiovascular complications caused by diabetes mellitus (Sangweni et al. 2019). The impaired metabolism of myocardial substrates corresponds to the increase of ROS, which leads to the aggravation of cell apoptosis and makes the heart susceptible to cardiomyopathy (Sun et al. 2013). In addition to the role of NADPH oxidase, the production of ROS in myocardial cells increases due to the damage of mitochondrial membrane potential, as described in several hyperglycemia studies (Su et al. 2016). A large number of studies have shown that apoptosis increases in the early and late stages of cardiac injury, suggesting that cell death may play a role in cardiac remodeling and subsequent development of cardiovascular diseases (Ge et al. 2016). *Panax notoginseng* saponin R1 is a compound with many pharmacological properties. It has been reported to improve complications associated with obesity, diabetes and cardiovascular disease. The role of notoginsenoside R1 in alleviating hypoxia and hypercapnia-induced

Table 2: Pharmacological actions of notogisengnoside R1 on cardiovascular diseases

Cardiovascular disease type	Causes of illness	Mechanism of action
Cardiac dysfunction	Lipopolysaccharide surge	Blockade of NF-k B activation (Sun et al. 2013)
Atherosclerosis	Restenosis caused by neointimal hyperplasia	Notoginsenoside R1's mode of action is through inhibiting the activation of phosphatidylinositol 3-kinase (PI3K)/Akt signaling.(Fang et al. 2018)
	ApoE Deficient	Mediated through its multiple targeting effects on inflammation, oxidative stress, lipid metabolism and microRNA expression. (Jia et al. 2014)
		Notoginsenoside R1 suppressed the expression of CC chemokine receptor 2 (CCR2) and prevented Ly6C(high) proinflammatory monocytes and the subsequent myocardial inflammatory responses and expression of various cell-derived factors around the cardiac wound. (Xiao et al. 2018)
	oxidized low-density lipoprotein	inhibiting ox LDL-induced NF-κB and MAPK activation (Su et al. 2016).
Hypertension	High sodium low potassium trigger	Induction of iNOS regulated by long non-coding RNA AK094457 (Yang et al. 2015)
Pulmonary arterial hypertension (PAH)	Pulmonary vasoconstriction	Inhibition of hypoxia–hypercapnia-induced vasoconstriction by the ERK pathway. (Xu et al. 2014)
		Increasing the production of t-PA and u-PA (Zhang and Wojta 1997b).
		Inhibits TNF-alpha-induced ERK activation and subsequent fibronectin overexpression (Yan et al. 2013)
Myocardial injury	Ischemia-reperfusion (IR)	Activation of the TGF-β1/TAK1 signaling pathway (Ge et al. 2016)
Diabetic encephalopathy	Oxidative stress and inflammation	Activating the Akt/Nrf2 pathway and inhibiting NLRP3 inflammasome activation(Zhai et al. 2018)

vasoconstriction and its related mechanisms. Yang et al. (2015) were the first to show the anti-atherosclerosis effect of notoginsenoside R1, which can be mediated by its multiple targeting effects on inflammation, oxidative stress, lipid metabolism and microRNA expression (Yang et al. 2015). Similarly, notoginsenoside R1 is a promising compound for protecting the heart from septic shock, possibly by activating ERalpha and PI3K/Akt signaling pathways. In conclusion, notoginsenoside R1 also plays an important role in protecting the cardiovascular system (as shown in Table 2).

This review clearly summarizes the evidence needed for the molecular mechanism of cardioprotective effects of maternal notoginsenoside R1. If more in-depth research and more reliable mechanism to open up the development of clinical value, this may be an important step to improve the market value of notoginsenoside R1.

4.3. Anti-colorectal-cancer activity

Colorectal cancer is also a major disease with high mortality. Studies have shown that *Panax notoginseng* has protective effects on colorectal cancer (Lassen et al. 2017). *Panax notoginseng* saponin R1 is an important component of Panax notoginseng, which is degraded by the intestinal microflora into active metabolites with chemical preventive effect (Awaysheh et al. 2017). In recent years, a large number of studies have shown that notoginsenoside R1 has pharmacological activities and beneficial effects on cancer, oxidation, etc. (Nichols et al. 2007; Han et al. 2007). A study has shown that notoginsenoside R1 can control colon tumors, protect actin filaments in cells and inhibit the proliferation and migration of advanced cancer cell lines (Chula et al. 2012; Lee et al. 2017). Ruan et al. (2010) found that notoginsenoside R1 can effectively promote the metabolism of the intestinal flora (Ruan et al. 2010). On the other hand, Liu et al. (2009) found that notoginsenoside R1 has a certain inhibitory effect on intestinal cancer. There have also been studies on the treatment of colon cancer by notoginsenoside R1. Within 24 h, the migration and invasion ability of HCT116 colon cancer cells decreased significantly with increased doses of notoginsenoside R1 (Zhang et al. 2015). A possible inhibitory mechanism of notoginsenoside R1 on colon cancer cells is shown in Fig. 2. However, besides HCT116 cells, there are human colorectal cancer (CRC) cell HCT8, HT29, LS174T (Horibe et al. 2018). Thus, further research is needed to study the mechanism of the effect of notoginsenoside R1 on different intestinal cancer cells in order to fully understand the protective effect of notoginsenoside R1 on the intestinal system.

4.4. Anti-inflammatory and inhibit inflammasome activation of notoginsenoside R1

Exogenous pathogens or chemicals can cause various types of inflammation and can damage human health, making the development of new carriers for the treatment of inflammation important (Yamada 2018). Long lasting inflammation certainly causes damage (Jayarathne et al. 2019). A large number of studies support the anti-inflammatory effect of notoginsenoside R1, as it has a certain effect on regulating cytokine production and pro-inflammatory gene expression (Zhang et al. 2008; Cheng et al. 2014). Active nuclear factor-kappa B (NF-kappa B) opens the expression of certain genes that increase the proliferation of affected cells and thus enhance the inflammatory response. *Panax notoginseng* saponin R1 inhibits the production of interleukin-1beta (IL-1beta) and tumor necrosis factor-alpha (TNF-alpha), both of which are pro-inflammatory cytokines (Agarwal et al. 2019). Similarly, one study found that notoginsenoside R1 inhibited the production of oxLDL-induced inflammatory cytokines by activating PPAR gamma, followed by PPAR gamma inhibiting or LDL-induced activation of NF-kB and MAPK (Wang et al. 2019). At present, although little research has been done on the anti-inflammatory effect of notoginsenoside R1, knowledge about in vivo efffects is still insufficient.

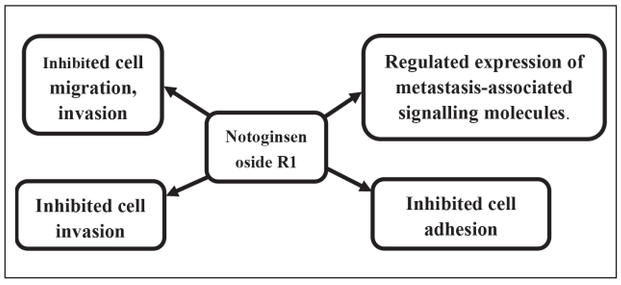

Fig. 2: Summary of the mechanisms of naturally occurring compounds with human colorectal cancer (CRC) cell metastasis. Naturally occurring compounds with human colorectal cancer effects occur through different mechanisms, such as Inhibiting cell migration invasion, regulating expression of metastasis-associated signalling molecules, Inhibiting cell invasion, Inhibiting cancer cell adhesion. The mechanisms of human colorectal cancer are involved cancer cell Inhibition and regulation.

However, the proposed anti-inflammatory effects of notoginsenoside R1 can play a role in drug design and targeting, as well as in the food and cosmetics industry. It may also provide possible treatment options for nflammatory diseases with minimal side effects.

4.5. Anti-organic-ischemic-reperfusion-injury activity

Ischemia of organs requires urgent reperfusion of tissue to restore organ function and transformation. Recent intra-arterial thrombectomy has shown to be a very encouraging treatment for patients with cardiac ischemia-reperfusion (Xiao et al. 2017; Sun et al. 2017). Traditional anti-angina drugs include nitrates, beta-blockers and calcium channel blockers, which are thought to improve myocardial oxygen balance by changing hemodynamic parameters. Unfortunately, these drugs itself can cause further damage to heart function (Boettcher et al. 2017; et al. Zheng 2018). Notoginsenoside R1 alleviates organ ischemia-reperfusion injury (Table 3). It is not difficult to find that myocardial, kidney and intestinal protective effect are more obvious. So far, however, there are no deep studies of microscopic changes in ischemic tissue, which may document the recovery of ischemia-reperfusion organs under treatment with notoginsenoside R1.

4.6. Anti-apoptosis activity of notoginsenoside R1

Resistance to apoptosis as the genetically programmed cell death (Ren et al. 2018) may seriously threaten human health (Russo et al. 2018; Suehiro et al. 2018). Some studies have found anti-apoptotic effects of *Panax notoginseng* saponin R1 *in vitro*. Xu and Wang (1991) have shown that human promyelocytic leukemia cells (HL-60) can be induced to differentiate into mature neutrophils (Xu and Wang 1991) by *Panax notoginseng* saponin R1. Recent advances have been made in the study of the anti-apoptotic effect of notoginsenoside R1. Notoginsenoside R1 attenuates glucose-induced podocyte injury (Huang et al. 2017b) by inhibiting apoptosis and activating autophagy *via* PI3K/Akt/m TOR signaling pathway.

Panax notoginseng saponin R1 inhibits the activity of CYP1A2, but had no effect on the activity of CYP2C11, CYP2D1 and CYP3A1/2. Potential herbal interactions between *Panax notoginseng* saponin R1 preparations and drugs as CYP1A2 substrates may be relevant (Ma et al. 2015). Estrogen receptor alpha mediates the effects of notoginsenoside R1 on endotoxin-induced inflammation and apoptosis in H9c2 cardiomyocytes (Yin et al. 2016). The possible anti-apoptotic mechanism (Fig. 3) can be inferred from many studies, which can more directly reflect the inhibitory effect of *Panax notoginseng* saponin R1 on cell apoptosis. Research is still in early stages, and clinical significance needs to be further studied.

Table 3: Pharmacological actions of notogisengnoside R1 on ischemia-reperfusion injury

Ischemic organs	Organ ischemia model in rats	Effective concentration/dose	Mechanism of action
Renal	Both left renal artery and vein were clamped by microaneurysm clamps for 45 min After the renal clamps were removed.	10mg/kg	P38 and nuclear factor .B inhibition. (Liu et al. 2010)
Cardiac	Clamped by cardiac for 30 min and reperfusion for 60 min.	20mg/kg	Inhibited p-IkB, NF-κBP65, p- NF-k BP65 protein levels and increased VDUP1 protein level. (Xia et al. 2015)
Instestines	The rats underwent a midline laparotomy, and the superior mesenteric artery (SMA) was isolated and clamped for 90 min with an atraumatic arterial clamp to occlude splanchnic circulation. After the renal clamps were removed.	10mg/kg	Its potential for modulation of energy metabolism and regulation of microvascular permea-bility. (Li et al. 2014)
	The superior mesenteric artery (SMA) of C57/BL mice was ligated for 15 min to induce gut ischemia followed by 30-min reperfusion.	20mg/kg	Its inhibition of leukocyte rolling and adhesion by inhibiting the expression of E-selectin in endothelium and CD18 in neutrophils. (Chen et al. 2008)
Cerebral	Using the bilateral common carotid artery occlusion (BCCAO) method	100mg/kg	Using the bilateral common Carotid artery occlusion(BCCAO)method (Zou et al. 2017)
		20mg/kg	Etrogen receptor-dependent activation of Akt/Nrf2 pathways (Meng et al. 2014b)
	HI was imitated by unilateral ligation of the common carotid artery (CCL) followed by 2.5 h of hypoxia in 7-day-old SD rats.	15 mg/kg	Promoting cell survival via the PI3K-Akt-mTOR/JNK signaling pathways by targeting ER in neonatal hypoxic–ischemic injury(Tu et al. 2018).
Lung	the coronary left anterior descending(LAD) branch was ligated and occluded for 30 min, and then released for myocardial reperfusion for 180 min; remote chemic ostconditioning (RIP) group	25mg/kg	Inhibiting the activation of the TGF-β1-TAK1 signaling pathway (Ge et al. 2016)

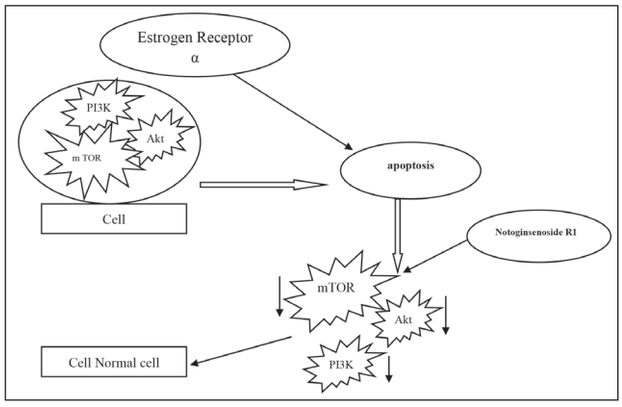

Fig. 3: The mechanisms anti-apoptosis by notoginsenoside R1. Notoginsenoside R1 alters apoptosis by regulating mTOR, AKT and P13K signaling factors. Direct actions of apoptosis. Direct action is mediated by interaction of a mTOR, AKT and P13K signaling factors, which induces regulation of cytokine

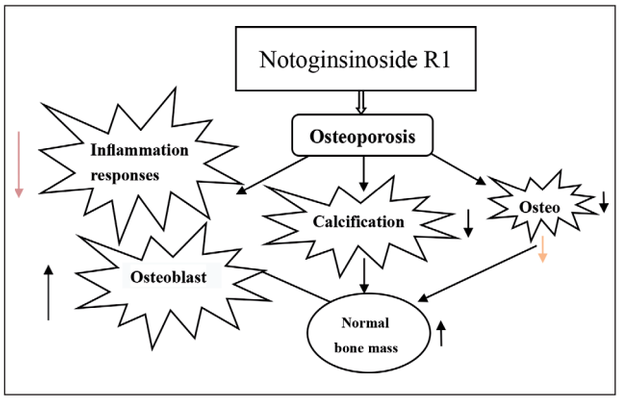

Fig 4: Pharmacological classification of mechanism of the expression on osteoporosis. Notoginsenoside R1 inhibits inflammatory reaction, promotes the formation of bone cells, and alleviates bone calcification, thereby inhibiting osteoporosis

4.7. Anti-osteoporosis activity

Osteoporosis is a group of bone diseases caused by a variety of causes. Thanks to the outstanding clinical effect and the patients' acceptance of the treatment results, joint replacement has become a treatment option. Bone regeneration is a coordinated activity of osteoblasts, which is coupled with bone remodeling of osteoclasts. For more than a thousand years, Chinese herbal medicines have been used to promote the recovery of fracture sites (Wang et al. 2016c; Bruyere et al. 2017; Lems 2017). Still, there is an urgent need for osteoporosis therapies. Current studies suggest that osteoblast lines may be different from primary osteoblasts or bone marrow stoma cells. It has been found that notoginsenoside R1 could exert anti-osteoporosis effects (Wang et al. 2015). Notoginsenoside R1 inhibited RANKL-mediated osteoclastogenesis and osteoclasts bone resorption. It may be a promising therapeutic agent for preventing periosteal osteolysis induced by wear particles (Lewiecki et al. 2018). Zhao et al. (2017) studied the role of NKL stimulation at the same time point, including NFATc1 and c-fos, which play an important role in osteoclastogenesis. NF-kappa B and MAPK signaling pathways have two key transcription factors. Notoginsenoside R1 significantly promotes osteoblast formation in pre-osteoblasts, suggesting that notoginsenoside R1 has potential as a bone regenerant. Sun et al (2007) found that notoginsenoside R1 can stimulate the production of bone cells through the signal transduction of hormone receptors. These studies have significance for the treatment of osteoporosis. Mechanistic considerations are summarized in Fig. 4).

4.8. Other pharmacological effects of notoginsenoside R1

Notoginsenoside R1 has also effects on other diseases in addition to the effects described above. Fan and Qiao (2017) have demonstrated that notoginsenoside R1 can effectively inhibit lipopolysaccharide-induced microcirculation accumulation in rats. Notoginsenoside R1 attenuates endothelial-induced high glucose-induced endothelial damage (Chen et al. 2017b). Administration of notoginsenoside R1 to animals can increase the retention and quality of antilogous fat grafts by increasing the vascular distribution at the receptor site (Jia et al. 2014). Notoginsenoside R1 plays an important role in the recovery treatment after fat transplantation. It can alleviate hypoxia-reoxygenation injury (Chen et al. 2018). These studies laid the foundation for the clinical research of notoginsenoside R1 in the treatment of lipopolysaccharide-related diseases.

5. Conclusion

This review summarizes pharmacological activities of notogisengside R1, which is rich in pharmacological properties. Modern studies have shown that steroidal saponins with significant anti-aging and anti-inflammatory activities are the main contributors to traditional pharmacological activities. We summarized current knowledge about the biological activities of notoginsenoside R1, including anti-osteoporosis, inhibiting human intestinal diseases, anti-inflammatory and cardioprotective effects. Heart protection patients often seek remedies from traditional medicinal plants, which have fewer side effects than traditional therapies (Zou et al. 2017; Zhong et al. 2015). However, current research still has considerable limitations, so only few studies have been conducted on the anti-apoptotic effect of notoginsenoside R1 and the treatment of osteoporosis. A large number of experiments are needed to clarify mechanisms of action. Although clinical trials with notoginsenoside R1 are also rare, more controlled trials should be conducted in the future. Meanwhile, notoginsenoside R1 has been approved by the Food and Drug Administration of China to start clinical arthritis prevention and treatment trials (Zhang and Wang 2006). At later stages, notoginsenoside R1 can also form the basis for cancer treatment. So far, however, it is difficult to make a definite decision on the clinical efficacy of *Panax notoginseng* saponins.

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