ISSN PRINT 2319 1775 Online 2320 7876

Research paper UGC CARE Listed (Group -I) Journal Volume 11, S Iss 4 ,2022

The Pharmacology of Ginsenosides: A Review

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ABSTRACT:

Ginsenosides, the active components of ginseng, have been demonstrated to modulate a wide range of physiological functions, lending credence to the herb's medicinal potential. Before illustrating how ginsenosides exercise their effects via interactions with steroidal receptors, this article will examine the structure, systemic transformation, and bioavailability of these compounds. Ginsenosides are valuable resources for the creation of new modalities due to their wide range of biological activities. But ginsenoside's poor bioavailability is a major barrier that must be solved before it can be widely used in clinical practise.

Keywords*:* Pharmacology, Ginsenosides

INTRODUCTION:

Background

In traditional Chinese medicine, Panax ginseng (Renshen, Chinese ginseng) is a staple herb that is often used alone or in combination with other medicinal components. The Greek term for "all-healing" inspired Russian botanist Carl A. Meyer to create the name Panax for the genus of plants in the Araliaceae family. P. ginseng, P. quinquefolium (Xiyangshen, American ginseng), P. notoginseng (Sanqi), and P. japonicus are just a few of the at least nine species that make up the Panax family (Japanese ginseng). In 2001, it was projected that the global sales of ginseng products would total US$ 300 million [1,2].

Reduced hypertension, increased metabolic rate, and enhanced immunological function have all been linked to ginseng use [3-6]. It wasn't until the isolation of ginsenosides in 1963 [7,8] that the plant's action mechanism was understood. Since then, a great deal of time and energy has been spent analysing the effectiveness of each ginsenoside and identifying the chemical mechanism by which they work. According to the Pubmed page, the number of articles on ginseng and ginsenosides has increased rapidly since 1975.

Ginsenosides are the pharmacologically active components in ginseng

Ginsenosides are saponins of the triterpene family. The majority of ginsenosides consist of sugar moieties (such as glucose, rhamnose, xylose, and arabinose) coupled to the C-3 and C-

ISSN PRINT 2319 1775 Online 2320 7876

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20 positions of a dammarane skeleton (17 carbons in a four-ring structure) [9,10]. In the naming of ginsenosides, the letter 'R' represents the root and the letter 'x' specifies the chromatographic polarity in alphabetical order [7]; so, the least polar molecule would be referred to as 'Ra,' while the most polar would be referred to as 'Rb. More than 30 different ginsenosides have been found, and they fall into two broad groups: (1) the 20(S)-protopanaxadiol (PPD) (Rb1, Rb2, Rb3, Rc, Rd, Rg3, Rh2, Rs1) and (2) the 20(S)-protopanaxatriol (PPT) (Re, Rf, Rg1, Rg2, Rh). PPDs deviate from PPTs in that they feature a carboxyl group at carbon six [9,10]. Additionally, some uncommon ginsenosides have been discovered, including ocotillol saponin F11 (24-R-pseudoginsenoside) [11] and pentacyclic oleanane saponin Ro (3,28-O-bisdesmoside) [12].

Extractions de ginsea normalisées

Researchers often employ standardised ginseng extracts that are available for purchase to eliminate inter-preparation variation. P. ginseng G115 (total ginsenoside adjusted to 4%) (Pharmaton SA, Switzerland) and P. quinquefolius NAGE (total ginsenoside content adjusted to 10%) are two of the most popular standardised extracts (Canadian Phytopharmaceuticals Corporation, Canada).

In high-performance liquid chromatography (HPLC) studies of these two ginseng extracts, ginsenosides Rb1, Rb2, Rc, Rd, Re, and Rg1 were discovered in both G115 and NAGE, but ginsenoside Rg2 was only found in G115. When comparing G115 and NAGE, we find that the former has a greater Rg1, while the latter has higher Rb1 and Re [12-14].

Chemical conversion of ginsenosides

Neuroprotection [19–13], antioxidation [14–16], regulation of angiogenesis , and cytotoxicity [10–12] are just some of the bioactivities discovered when treating different cultured cells with ginsenosides. To be functional in mammalian systems, ginsenosides may first need to undergo biotransformation. Biological effects of ginsenoside metabolites were found to be larger than those of ginsenosides in recent research [13–15]. The ginsenoside Rg3's metabolites, Rh2 and PD, have more strong anti-tumor effects [14].

Intestinal metabolites of PPTs and PPDs, substance K, PT, and PD, inhibit human liver enzyme cytochrome P450, although ginsenosides Rb1, Rb2, Rg1, and Re do not [15].

Pharmacokinetic and bioavailability of ginsenosides

The mechanisms by which ginsenosides, both in their original and altered forms, are absorbed and delivered to the human system, are not well understood. Ginsenosides require energy and exhibit non-saturable transport across the intestinal mucosa [17, 19]. There may be a role for the sodium-dependent glucose co-transporter 1 in this [20]. Intact ginsenosides and their metabolites are only barely absorbable from the intestines [11-13]. As an illustration, after oral treatment of ginsenosides, only 3.29 percent Rg1 and 0.64 percent Rb1 are identified in rat serum [18,19], corroborating the classic experiments by Odani et al. in 1983 [14,15]. Within 24 hours of oral ingestion, Rg1 levels become undetectable, while Rb1

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Pharmacokinetic and bioavailability of ginsenosides

Various receptors, including receptor tyrosine kinases (RTK) [21], serotonin receptors (5-HT) [22], NMDA receptors [23], and nicotinic acetylcholine receptors (AChR) [14], have their expressions and functions altered by ginsenosides. Only steroid hormone receptors have been shown to have direct interactions with ginsenosides at the receptor ligandbinding sites; ginsenosides Rg1 [18] and Re [26] are functional ligands of the glucocorticoid receptor (GR), while ginsenosides Rh1 and Rb1 are functional ligands of the oestrogen receptor (ER), in particular the ER These results explain why ginsenosides exacerbate menopausal symptoms and how the endocrine system is modulated with long-term ginseng use [3,4].

As a stress hormone, glucocorticoid stimulates GR to initiate the body's ‘fight or flight’ response. How does ginseng work as an adaptogen and stress reliever if Rg1 and Re are GR ligands? It's possible that Rg1 and Re act as GR partial agonists. When ginsenosides are present in excess, Rg1 and Re both block the binding of the synthetic glucocorticoid dexamethasone to GR, with complete displacement being feasible [16,17].

The fact that Rg1 and Re stimulate GR-dependent biological processes that are sensitive to the GR inhibitor RU486 indicates that these ginsenosides are agonists for GR rather than inhibitors [18,16]. These ginsenosides are likely to be partial agonists of GR due to the fact that their steroidal actions are not as pronounced as dexamethasone's. When the intrinsic

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ligand is lacking or insufficient, ginsenosides may serve to compensate for the lack of steroidal activity under physiological settings. However, when present in high enough quantities, ginsenosides can occupy a portion of the steroidal receptor with low affinity and therefore block the actions of steroids.

Further, each ginsenoside can connect to several different steroid hormone receptors. Cross-talk between ginsenoside Rg1 and the insulin-like growth factor-1 receptor (IGF-IR) occurs in neural cells via the endocannabinoid system [11]. ER alpha isoform, androgen receptor, and progesterone receptor are involved in the effects of ginsenoside Re on cardiac myocytes [12]. It has been shown that the endometabolites PD and PT bind to and activate both GR and ER in endothelial cells [13]. Several potential benefits of ginseng may be attributable to the compound's ginsenosides' ability to act on multiple target receptors.

CONCLUSION

Ginsenosides, as partial agonists to many steroidal receptors, are a major natural resource to be developed into novel modalities, and may one day replace steroids in the existing regimen, reducing unwanted side effects. However, when ginsenosides and its metabolites are taken orally, only a small percentage of the dose reaches the target biological system due to poor bioavailability. Only when (1) pure compounds of the ginsenosides are available in sufficient quantities, (2) the ginsenosides are biochemically stabilised to avoid degradation and enhance absorption in the gastrointestinal tract, and/or (3) special delivery methods for the ginsenosides reach the areas of treatment will the results of ginsenoside researches become physiologically relevant. Furthermore, this review underlined the need for ginsenoside transformation in order to exercise its greatest benefits in the mammalian system; hence, enhancing this transformation would aid in optimising the restorative effects of ginsenosides. If these two concerns could be resolved soon, it would be a huge step forward for ginseng studies and the prospect of clinical application.

Acknowledgements

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