

## Investigate potential interaction between herbal products and conventional medication

Arnav Sharma<sup>1</sup>, Ashima Ali<sup>1</sup>, Asheesh Walia<sup>1</sup>, Ayush<sup>1</sup>, Ms. Nancy Sharma<sup>2</sup>

<sup>1</sup>Student, Abhilashi College of Pharmacy, Nerchowk, Mandi 175008 (H.P)

<sup>2</sup>Assistant Professor, Abhilashi College of Pharmacy, Nerchowk, Mandi 175008 (H.P)

Corresponding Author: Arnav Sharma

Date of Submission: 06-05-2026

Date of Acceptance: 17-05-2026

### Abstract:

There are serious worries about potential herb-drug interactions due to the growing usage of herbal items in conjunction with prescription drugs. Many herbal remedies contain bioactive substances that can affect the pharmacokinetics and pharmacodynamics of conventional medications, despite the fact that they are frequently regarded as natural and safe. Reduced medication efficacy or an increased risk of side effects could result from such interactions. By examining current scientific research and clinical data, this study looks into possible interactions between widely used herbal items and prescription drugs. It focuses on processes including altered drug metabolism, enzyme stimulation or inhibition, and modifications to drug absorption and excretion. Additionally, the study assesses the possible influence of often reported interacting herbs on therapeutic effects. To guarantee safe drug practices, patients and healthcare providers must comprehend these connections. The results highlight the need for further patient education, awareness, and research to reduce the hazards of using conventional and herbal drugs at the same time.

### Key Points:

- Herbal products are frequently used in conjunction with prescription drugs.
- Bioactive chemicals found in many herbs have the potential to interact with prescription medications.
- Herb-drug interactions can change how drugs are absorbed, metabolized, distributed, or eliminated.
- These interactions may make drugs less effective or more harmful.
- Enzyme induction or inhibition (liver enzymes, for example) are common ways
- Patients' and healthcare providers' ignorance raises the possibility of negative consequences. •Disclosure of herbal use and appropriate patient counseling are crucial.
- To guarantee the safe combination of herbal and conventional drugs, further clinical research and regulation are required.

### I. Introduction:

•As interest in natural and alternative medicines has grown, so has the use of herbal products globally. Herbal remedies are widely used to promote health, prevent disease, and treat a variety of ailments. These products are frequently used without medical supervision and are readily available. Conventional drugs continue to be the mainstay of treatment for numerous illnesses. Because of this, a lot of people combine herbal remedies with over-the-counter or prescription medications.

•Herbal remedies contain biologically active substances that may interact with prescription drugs, despite the fact that they are frequently thought to be harmless because they come from natural sources. The pharmacokinetics and pharmacodynamics of drugs can be changed by these interactions, also referred to as herb-drug interactions. Drug absorption, distribution, metabolism, and excretion may be impacted by such modifications, which could result in decreased therapeutic efficacy or a higher risk of side effects.

•Furthermore, older adult populations are generally more inclined to use both herbal remedies and mainstream pharmacological therapy.

•Additionally, there is a greater likelihood of chronic illness in this demographic, which frequently necessitates the use of increasingly complicated conventional medication therapy. As a result, there is a greater chance of herb-drug and herb-disease interactions in older adult populations. Research assessing the use of herbal medications is still lacking, particularly clinical studies. This, together with the continuous creation of novel conventional medication treatments, further When components of these two therapy techniques are combined, the number of unknown outcomes increases. Herbal remedies are not as strictly controlled as traditional pharmacological therapy in many nations, including the United States

• Additionally, globalization has made herbal remedies from all over the world much more accessible to individual consumers. Coordinated efforts are obviously needed to carry out the required clinical trials to investigate the safety and effectiveness of herbal remedies, both on their own and in combination with traditional medication therapy.

• A number of popular herbs, including garlic, ginkgo biloba, and St. John's Wort, have been shown to interfere with some prescription medications. For instance, some herbs may increase or decrease the pharmacological effects of drugs, while others may activate or inhibit liver enzymes involved in drug

metabolism. Particularly for patients receiving medications with a limited therapeutic index, these interactions can present serious hazards.

• Patients and healthcare professionals are still not well-informed about possible herb-drug interactions, despite the growing usage of herbal remedies. As a result, it's critical to look into potential interactions between herbal products and prescription drugs. Comprehending these relationships can enhance patient safety, direct medical practitioners in their clinical work, and facilitate the creation of more effective regulatory and educational initiatives for the safe combination of conventional and natural medications.

## II. Literature Review:

### 1. Common herbal products and their interactions:

Herb	Botanical species	Traditional and modern clinical use	Form(s) of HMP	Known effects on drug metabolising enzymes and P-gp	Clinical and pharmacological interaction reports	Recommendations based on clinical evidence or sound theoretical grounds
<b>Ashwagandha</b>	<i>Withania somnifera</i>	tonic, sedative, and anti-inflammatory	Root extract	NK	increases the sedative effects of certain benzodiazepines (Kulkarni SK, George B, Mathur R, 1998) and barbiturates (Rao A, Karanth KS, 1990).	As a precaution, avoid usage alongside benzodiazepines and other sedatives.
<b>Cinchona</b>	<i>Cinchona</i> species	Bitter tonic (containing quinine, an antimalarial)	Bark extract	Unlike isolated alkaloids, low concentrations of quinine in tonic water do not inhibit CYP2D6 in vivo. Unlike isolated alkaloids, low concentrations of quinine in tonic water do not inhibit CYP2D6 in vivo.	NR	None are known to have low quinine levels.
<b>Cloves</b>	<i>Eugenia caryophyllum</i> = <i>Syzygium aromaticum</i>	stimulant, antiseptic, and analgesic	Essential oil with flowerbud extract	In vitro, extracts inhibit human CP3A4, CYP2D9, and CYP2C9.	NR	NK
<b>Echinacea</b> (Purple Coneflower) and other species	<i>Echinacea purpurea</i> (also <i>E. pallida</i> ; <i>E. angustifolia</i> )	Immune stimulants, particularly for colds, flu, and URTIs	Herb and root extract Juice that has been	<i>E. purpurea</i> has been shown to inhibit human CYP3A4 in	NR. Results may not apply to all <i>Echinacea</i> species because they differ	Until more information is known, exercise caution when using medications that are substrates of CYP3A4

			freshly pressed	vitro (Budzinski JW, Foster BC, Vandenhoeck S, Arnason JT,2000); it decreased oral clearance of CYP1A2 substrates but not CYP2C9 or CYP2D6. CYP3A enzymes were selectively altered in vivo in animals based on the site (Gorski JC, Huang S-M, Pinto MD ET AL,2004).	somewhat chemically from one another.	and CYP1A2, such as several cancer treatments, phenytoin, warfarin, clozapine, theophylline, and midazolam.
<b>Garlic</b>	Allium sativum	antibacterial, antiplatelet, and hypercholesterol. FOOD	Bulb oil, powdered, dried, and occasionally aged	reduction of CYP2E1 activity in humans (Lin YC, Bioteau AB, Ferrari LR, Berde CB,2004), and certain animal species; some rise in CYP2B1/2, depending on the species (not humans) (Zhou S, Gao Y, Huang M, XU A, Paxton JW,2003); inhibition of CYP 3A4 in vitro; and suppression of P-gp in vitro S, (Foster BC, Foster MS, VandenhokS et al 2001).	Warfarin (Williamson EM 2003), lisinopril, (Mccoubrie M 1996), and chlorzoxazone, (Sparreboom A, Cox MC, Acharya MR, Figg W,2004) decreases the bioavailability of ritonavir and saquinavir, two protease inhibitors (Zhou S, Lim LY, Chowby B, 2004). seems safe when taking most medications, with the possible exception of saquinavir.	Warfarin should be used to monitor INRs. Protease inhibitors and the muscle relaxant chlorzoxazone should not be taken together.
<b>Ginger</b>	Zingiber officinalis	Food, antiemetic, carminative, and anti-inflammatory	Extracts from both fresh and dried rhizomes	In vitro, extract mildly inhibits CYP3A4, CYP2D9, and CYP2C9.	NR	NK
<b>Ginkgo</b>	Ginkgo biloba	Boost blood flow to improve memory and cognition in erectile dysfunction, intermittent	extract from leaves. Fruit consumed in China	In vivo human CYP1A2, CYP3A4, CYP2E1, and CYP2D6 activity is unaffected (Lin YC,	Omeprazole, in Chinese patients (Sparreboom A, Cox MC, Acharya MR, Figg W, 2004); rofecoxib, trazodone,	Warfarin should be used to monitor INRs. Use caution when taking trazodone, donezepil, alprazolam, or antiplatelet medications like aspirin. Steer clear

		claudication, and dementia		Bioteau AB, Ferrari LR, Berde CB,2004). CYP1A family inhibition in rats (Smith L, Ernst E, , Ewings P, Myers S, Smith C, 2004). Rats had higher levels of CYP3A1 and CYPB1/2 (Ernst E ,2003). modest human CYP2C19 inducer in vitro	alprazolam, donezepil, and warfarin (Williamson EM, 2003; Galluzi S, Nanetti O, Binetti G et al, 2000); aspirin (data contradicting, same adverse effects attributed to aspirin alone); and numerous reports of ginkgo interactions deemed "exaggerated"	of anticancer medications
<b>Ginseng</b>	Due to its high cost, <b>Panax ginseng</b> is highly susceptible to fraud, particularly when combined with liquorice (qv). (P. quinquefolius is American ginseng.)	weariness, both mental and physical; increase virility	Root extract could undergo fermentation	Ginsenosides moderately inhibited P-gp (measured using multi-drug resistant cell lines), but only at high concentrations; inhibition in human and mouse ribosomes of CYP2E1; varied enzyme selective effects on other CYPs depending on the nature of extract (Zhou S, Lim LY, Chowbay B, 2004); and no effect on CYP activity in one human study (Lin YC, Bioteau AB,Ferrari LR, Berde CB,2004).	American ginseng decreased the effects of warfarin in healthy volunteers (Jones BD, Runikis AM, 1987), in contrast to Asian ginseng; potentiated phenelzine (MAOI) (Williamson EM, 2003; Budzinki JW, Foster BC, Vandenhoeck S, Arnason JT, 2000; Jones BD, Runikis AM, 1987), and nifedipine (a CYP3A4 substrate) , (Zhou S, Gao Y, Huang M, XU A, Paxton JW, 2003).'	Steer clear of nifedipine, MAOIs, and cancer chemotherapy. Use benzimidazoles with caution. Warfarin should be used to monitor INRs.
<b>Green tea</b>	Camellia sinensis	Food, chemoprotectant, and antioxidant	leaf infusion (tea) Leaf extract	CYP2A6, CYP2C19, CYP2E1, CYP3A4, and P-gp are all inhibited by catechins. CYP1A2 is induced by caffeine	NR. The chemoprotective effect is believed to be caused by inhibition of certain CYP enzymes. In healthy volunteers, green tea extract had no effect on CYP3A4 or 2D6.	NK

<b>Kava*</b>	Piper methysticum	Anxiety	Root extract	strong CYP3A4, CYP1A2, CYP2C9, CYP2D6, and CYP2C19 inhibitor	Alprazolam	It is no longer advised. Steer clear of sedatives and anticancer medications, many of which are metabolized by CYP3A4.
<b>Liquorice</b>	Glycyrrhiza glabra, G. uralensis	Food, carminative, and expectorant	Rhizome (or "root") extract	increases the activity of CYP3A enzymes, CYP1A2, and CYP2B1 in rodents following repeated administration (Zhou S, Gao Y, Huang M, XU A, Paxton JW, 2003); nevertheless, in vitro, the extract demonstrated modest inhibition of CYP3A5 (Budzinski JW, Foster BC, Vandenhoeck S, Arnason JT, 2000). inhibits 11 beta dehydrogenase and 5 alpha and 5 beta reductases.	NR, but it might slow down the metabolism of other steroid medications. influences blood sugar levels and may cause problems for hypoglycemic medication	Steer clear of frequent, high dosages when taking steroid medications, such as oral contraceptives. Use caution when taking oral antidiabetic medications.
<b>Rosemary</b>	Rosmarinus officinalis	food, antiseptic, and memory booster	Extract from herbs	P gp inhibition in vitro (Deferme S, Augustijns P, 2002), (tested using drug-resistant P gp-expressing cell lines)	NR	NK
<b>St John's wort</b>	Hypericum perforatum	Seasonal affective disorder; mild depression	Complete extract	notable CYP2E1 (Lin YC, Bioteau AB, Ferrari LR, Berde CB, 2004), CYP3A4, CYP1A2, CYP2D6, and CYP2C19 induction; in vitro and in vivo P-gp induction	Digoxin, oral contraceptives, cyclosporin, simvastatin, methadone, fexofenadine, irinotecan, indinavir, tacrolimus, SSRIs, alprazolam, amitriptyline (Gurley WJ, Gardner SF,	high possibility for communication. Steer clear of digoxin, opiates, anticoagulants, immune suppressants, antineoplastics, protease inhibitors, fexofenadine, statins, omeprazole, verapamil, and other antidepressants.

				<p>(Sugomoto K, Ohmori M, Tsuruoka S et al, 2001; Zhou S, Chan E, Pan S-Q, Huang M, Lee EJ, 2004). Competing effects: SJW first inhibited P-gp before inducing it (Wang EJ, Barecki-Roach M, Johnson WW,2004).</p>	<p>Hubbard MA et al, 2002; Hebert MF, Park JM, Chen Y-L, Akhtar S, Larson AM, 2004; Wang LS, Zhou G, Zhu B et al, 2004), omeprazole, verapamil (Sparreboom A, Cox MC, Acharya MR, Figg W, 2004; Tannergren C, Engman H, Knutson L, Hedeland M, Bondesson U, Lennernas H, 2004; Morimoto T, Kotegawa T, Tsutsumi K, Ohtani Y, Imai H, Nakano S, 2004), and theophylline (Zhou S, Chan E, Pan S-Q, Huang M, Lee EJ, 2004). had no effect on human subjects' serum theophylline levels (via CYP1A2) (Markowitz JS, Donovan JL, Devane CL et al, 2003).</p>	
<b>Turmeric</b>	Curcuma longa	Food, liver problems, and rheumatism infections	powdered rhizome, or "root"; rhizome extract	<p>CYP3A4, CYP2D9, and CYP2C9 are inhibited by extract (Butterweck V, Darenforf H, Gaus W, Narstedt A, Schulz V,Unger M,2004). Although curcumin inhibits P gp, its oral bioavailability is quite low (Zhou S, Lim LY, Chowbay B , 2004).</p>	<p>NK. Patients on large dosages of anticoagulants or antiplatelet medications should exercise caution.</p>	NK

### III. Mechanism of interaction:

#### Type of Interactions:

- **Pharmacokinetic Interactions:**

In this, herbal drug alters the ADME i.e. absorption, distribution, metabolism, protein binding or excretion of drugs resulting into alteration in the level of drug or its metabolites (Pasi, 2013; Mamindla et al.,2016). Current evidences report that most of the herbal drug interactions are correlated to oxidative metabolism by (CYP)cytochrome P450 system and by the influence of an herb on the efflux drug transporter P-glycoproteins (P-gp) (Izzo,2005).

- **Pharmacodynamic Interactions:**

These are pertaining to the pharmacological activity of the interactive agents, and may affect organ system, receptor site or enzymes. Pharmacodynamic interactions may be additive (or synergistic), i.e., the herbal medicines improve the pharmacological / toxicological actions of synthetic drugs or antagonistic, i.e., the herbal medicine lessens the effectiveness of synthetic drugs. Interactions of warfarin are established illustration of such type of interactions (Holbrook et al., 2005). Elevated anticoagulant effect could be anticipated when warfarin is administered with anticoagulant herbs/ or with antiplatelet herbs like Garlic, Ginger, Ginkgo biloba etc.

The increasing use of Herbal medicinal products with prescribed drugs has raised issues related to quality, safety and efficacy of these products and may lead to life-threatening adverse effects. Moreover, amongst patients taking prescription medicines in US, 16% adopted herbal drugs as well (WHO, 2003). There has been widespread use of herb in the form of dietary

supplement for the management of various disorders. Previous reports have shown that that some of herbs such as St John's wort, Garlic, Ginseng, and Ginkgo, have given rise to clinical interactions when co-administered with prescription drugs. This review compiles all possible interaction of some commonly used herbal products with a number of prescription and OTC drugs.

- **Garlic:**

Garlic contains sulphur-based compounds called Alliin which is odorless chemical derived from the amino acid cysteine. It is further converted into allicin and finally into ajoene, strongly smelling compound. The ajoene has ability to prevent formation of clots in blood vessels and treatment of atherosclerosis (Lawson and Wang, 2005). It also contains peptides, terpenoids, flavonoids, phenol derivatives and various enzymes in minute proportions along with protein, fat, crude fibre, potassium, iron, magnesium etc (Odebunmi et al., 2009). Garlic is useful in skin diseases, arthritis, lumbago, backache, chronic fever, malaria, tuberculosis, urinary diseases, diabetes, kidney stones, anaemia, epilepsy, etc. Allicin and other compounds possess antihypertensive, hypolipidaemic, hypocholesterolemic and antithrombotic effects. Sulphur compounds in Garlic also have anticarcinogenic properties. These also prevent arteriosclerosis (Chan et al., 2013). Interaction of Garlic with antihypertensives and antidiabetics is mostly pharmacodynamic whereas that with anticoagulants, antivirals and Bordia, A. (1978). Effect of garlic on human platelet aggregation in vitro. Atherosclerosis, 30(4):355-360. antitubercular is pharmacokinetic.

#### Interactions of garlic with prescribed medications:

S.NO	Drugs	Potential Effects	Mechanism	Reference
1	With warfarin (anticoagulant drug)	Garlic inhibits platelet function and increases the bleeding risk.	Inhibits CYP3A4 and effects the plasma concentration of warfarin.	(Bordia, 1978; Rahman and Billington,2000
2	With atorvastatin (antihyperlipidemic drug)	Enhances the plasma concentration of drug leading to increased lipid peroxidation which will damage the kidney thereby increases the risk of nephrotoxicity.	Inhibition of CYP3A4	(Reddy et al., 2012)
3	With glibenclamide (antidiabetic Drug)	Increased hypoglycemic effect	Pharmacodynamic interaction	(Poonam et al., 2013)

4	With atenolol (βblocker)	Garlic interacts with atenolol resulting in reduced serum LDH and CK-MB activity (an increase of CK-MB is found in hypertensive patient)	Synergistic action/ Pharmacodynamic interaction	(Avula et al., 2014)
5	With Propranolol (βblocker)	Synergistic antihypertensive action	Pharmacodynamic interactions	(Asdaq et al., 2010)

➤ **Ginkgo Biloba**

Ginkgo biloba (family Ginkgoaceae), or Maidenhair is one of the most frequently available OTC herbal medicinal product in Germany and United states (Diamond et al., 2000). Ginkgo seeds and extract play a vital role in the TCM Pharmacodynamic and pharmacokinetic interactions of herbs with prescribed drugs: A review 187 (Traditional Chinese Medicines) and are widely illustrated as popular dietary supplements in Europe (DeKosky et al., 2008). It is used to treat anxiety, dementia and other vascular disorders especially alzheimer disease (Ihl et al., 2011). It also has the ability to improve blood circulation and improves psychomotor function (Ponto and Schultz, 2003). It is also used in Schizophrenic patients as an adjunct therapy to

antipsychotic drugs (Chen et al., 2015). Ginkgo biloba contains a wide number of phytoconstituents such as alkylphenols (ginkgolic acids), flavonoids (bilobetin, ginkgetin, quercetin, etc.) and terpenoids (bilobalides, ginkgolide A, ginkgolide B, ginkgolide C, ginkgolide J, etc.) and organic acids (6-hydroxykynurenic acid Ginkgolide (mainly ginkgolide B) are potent inhibitors of PAF-induced thrombocytopenia and constriction of bronchioles (Xin et al., 2015). G. biloba extracts and their constituents are inhibitors and inducers of drug-metabolizing CYP enzymes and transporters (Unger, 2013). Ginkgo leaves also contains ginkgotoxin, a B6 antivitamin which may cause epileptic seizures and other severe neuronal disorders, even death (Kajiyama et al., 2002).

**Interactions of Ginkgo Biloba with other prescribed medications.**

S. No	Drugs	Potential effects	Mechanism	references
1	With NASIDS	Spontaneous bleeding, may cause fatal intracerebral haemorrhage	Ginkgo reduces aggregation of platelet by rising concentrations of endothelium-derived thrombolytics	(Diamond et al., 2000; Bent et al., 2005)
2	With nifedipine (calcium channel blocker)	Reduced hypotensive action	Induction CYP3A	(Yoshioka et al., 2004)
3	With omeprazole (A proton Pump Inhibitor)	Reduced plasma drug concentration level due to increased clearance.	Induction CYP2C19	(Yin et al., 2004)
4	With losartan (first nonpeptide angiotensin-II receptor blocker)	Enhanced plasma drug concentration due to reduced metabolism.	Inhibition of CYP450 enzyme system.	(Klishadi et al., 2015; Wang et al., 2016)
5	With tolbutamide (hypoglycemic drug)	Enhanced Bioavailability and improved antidiabetic effect	Inhibition of CYP2C9 Activity and P-gp.	(Sugiyama et al., 2004; Uchida et al., 2006)

➤ **Ginseng:**

Ginseng is amongst the most popular herbal medicinal plant used as immunomodulator in

countries including Korea, Japan and China (Wang et al., 2015). Among various ginseng species, Asian ginseng (Panax ginseng) and American ginseng

(Panax quinquefolium), family Araliaceae are the most widely used species. Ginseng has been used to improve concentration, counteract Alzheimer disease; increases work efficiency and stamina with better wellbeing (Wang et al., 2012). It also has the ability to stimulate CNS to modulate immune system and anabolic effects, thus also known as immunomodulator or adaptogen (Nocerino et al., 2000). Ginseng is known to have varied pharmacological actions such as antifatigue, antiaging, antidiabetic, anticancer (Attele et al., 1999; Yuan et al., 2012). Various classes of constituents present in ginseng are saponin glycosides (ginsenosides or panaxosides derivative of aglycone protopanaxadiol, protopanaxatriol and oleanolic acid); polysaccharides (water soluble and

include panaxane A to U); Polyynes (Panaxynol, panaxytriol) and Volatile oil (α-bisabolol, thujopsene, α-cadinol) (Christensen, 2008). Naturally occurring ginsenosides may affect hepatic P450 activity in vivo by means of ginseng's intestinal metabolites. Ginsenoside metabolites are reported to inhibit the enzyme activities of CYP2A6, CYP2C9 and CYP3A4 (Liu et al., 2006; Kim et al., 2016). Ginseng extract also inhibited CYP1A1, 1A2, and 1B1 activities in recombinant human CYP isozyme system (Chang et al., 2002). Clinical pharmacokinetic studies in humans revealed that interactions of P. ginseng with drugs appear to be rare but still close monitoring is advised for patients consuming CYP3A or P-gp substrates with narrow therapeutic indices (Ramanathan and Penzak, 2017).

**Interactions of Ginseng with other prescribed medications:**

S. NO	Drugs	Potential effects	Mechanism	Reference
1	With warfarin (anticoagulant drug)	Reduced anticoagulant effect and decreases plasma drug concentration level as a result bleeding risk also increases.	Induction of CYP450 enzyme system	(Janetzky and Morreale, 1997; Vaes and Chyka, 2000)
2	With alcohol	Ginseng relieves the symptoms of alcohol hangover.	Ginseng decreased plasma ethanol concentration by delaying gastric emptying	(Koo, 1999; Lee et al., 2014)
3	With phenelzine MAO inhibitor (antidepressant drug)	Concomitant use of Ginseng with phenelzine may cause excess of stimulation leading to side effects like anxiousness, restlessness and insomnia.	Inhibition of cAMP phosphodiesterase and thus increase cAMP level.	(Stancheva and Alova, 1993; Jones and Runikis, 1987)
4	With imatinib (anticancer drug)	Hepatotoxicity was observed in 26 years old man with chronic myelogenous leukaemia when ginseng is simultaneously taken with imatinib.	Ginseng may inhibit CYP3A4 concerned in metabolism of Imatinib.	(Bilgi et al., 2010)

➤ **Green Tea:**

GT has main properties that can lead to drug interaction at different levels whose main chemical components are tea polyphenols (30% dry weight). Polyphenol compounds in GT have lots of catechins and catechins including EGCG, epicatechin-3-gallate (ECG), epicatechin (EC), and epigallocatechin (EGC). EGCG has the highest frequency among green tea polyphenols. The EGCG content of GT can

be a source of different interactions with drugs discussed below. Methyl xanthine's and purine alkaloids found in plants are found in beverages (coffee, tea, cocoa) consumed worldwide. Methyl xanthine's can be cause of different interactions, too. There are different types of drug interactions with GT. These GT-drug interactions can be classified as resulting from either a change in the drugs

pharmacokinetic and pharmacodynamics parameter. (Meyboodi M,2020 Dec 28: 196-203).

**Interactions of Green tea with prescribed medications:**

S. NO	Drugs	Amount of Green tea	PK and PD outcomes	reference
1	Amoxicillin	0.5 g powdered green tea extract.	Not significantly decreasing AUC but Cmax decreasing significantly.	Kiss. T et al, 2019;20(1):54.
2	Warfarin	NA	Probably increasing the bleeding time	Al-Arifi MN, Wajid S,2016.
3	Melatonin	15mg/kg of caffeic acid and quercetin	Increasing AUC & decrease plasma clearance	Jana S, Rastogi et al Jana S, Rastogi HH,2017.
4	Doxorubicin	25mg/kg	Increasing doxorubicin concentration in the cancer cell	Jiang X, Sun Y, Shang L, 2019.

**3. Clinical Implementations:**

• **Altered Drug Efficacy:**

When a herbal product alters the way a prescription medication is absorbed, metabolized, or eliminated, this is known as altered drug efficacy in herb-drug interactions. Either too little drug action or too much toxicity results.

The three primary ways that herbs interfere with medication efficacy are as follows:

1. CYP450 enzymes alter metabolism.

Liver enzymes, particularly CYP3A4, CYP2D6, and CYP2C9, break down the majority of medications. These can be stimulated or inhibited by herbs. \* Induction = quicker drug clearance = less efficacy A potent CYP3A4 + P-gp inducer is St. John's Wort. lowers blood levels of several cancer medications, birth control pills, cyclosporine, warfarin, and HIV medications. It has caused people to become pregnant or refuse transplants. \*Inhibition = slower medication clearance = increased risk of toxicity

CYP3A4 in the stomach is inhibited by grapefruit juice. may increase statin levels five to ten times, increasing the risk of rhabdomyolysis. impacts buspirone, felodipine, and some statins as well. Inhibit CYP3A4/2D6 with goldenseal and echinacea. can raise dextromethorphan and metoprolol levels.

2. \* Pharmacodynamic effects: larger or lower effect, same target

The drug and herb function via the same route. Platelets are inhibited by ginkgo, garlic, ginger, and warfarin/NSAIDs. Even if the INR appears normal, the combined result is a greater risk of bleeding. Benzodiazepines, kava, and valerian all result in CNS

depression and severe sedation. \*Licorice + Antihypertensives\*: Licorice lowers the effectiveness of blood pressure medications by causing salt retention. \*Ginseng + Warfarin: Ginseng may lower INR, which lowers the risk of clotting and anticoagulation.

**Aim and Objective:**

**Aim:** By recognizing, comprehending, and controlling the hazards connected to the concurrent use of herbal products and conventional medications, the main goal of researching herb-drug interactions (HDI) is to guarantee patient safety and optimize therapeutic outcomes.

**Objectives:** The inquiry usually concentrates on a number of important technical and clinical goals in order to accomplish this goal:

1. Determining Pharmacokinetic Interactions: to ascertain how herbal remedies affect how a traditional medication is processed by the body. Examine whether herbal ingredients, such as fiber or tannins, improve or impede the gastrointestinal tract's ability to absorb medications.

Metabolism: Examine how Cytochrome P450 (CYP450) enzymes are induced or inhibited. For instance, CYP3A4 is known to be induced by St. John's Wort, which can reduce the plasma concentration of numerous medications.

Excretion: Assess variations in renal clearance or transport protein activity, such as P-glycoprotein (P-gp).

2. Pharmacodynamic Interaction Assessment:

To evaluate the impact of the herbal medication on the conventional medicine's genuine pharmacological reaction.

Synergistic Effects: Determine whether the herb intensifies the medication's effects to a hazardous degree (for example, taking garlic or ginkgo biloba with anticoagulants like Warfarin increases the risk of bleeding).

Antagonistic Effects: Determine whether the herb lessens the medication's effectiveness (for example, ginseng may lessen the efficiency of several immunosuppressants).

3. Evaluation of High-Risk Populations:

To concentrate on groups where interactions may endanger life or result in treatment failure.

Chronic Conditions: Examine interactions in patients using "narrow therapeutic index" medications (such as cardiac medications, chemotherapy, or anti-seizure medications).

Vulnerable Groups: Examine the particular effects on young patients, pregnant women, and the elderly.

4. Database creation and clinical documentation:

To provide evidence-based guidelines and go beyond "theoretical" concerns.

Correlation: To verify real dangers in humans, connect in vitro (laboratory) results with in vivo (clinical) data.

Education: Give medical professionals verified information so they can advise patients and change medications as needed.

Methodology:

(a) Systematic review of literature and selection of potentially interacting herbs:

For this study, we identified safety reviews on herbal plants (Tandon 2018) as a valid source for required scientific evidence with direct reference to original research articles. For confirmation of the given data in the safety reviews, we cross-checked using online scientific literature search tools. Although many herbal medicinal plants were listed in the extensive book on safety reviews, we selected herbs based on reported safety testing and interaction with allopathic drugs only. Seventy-four original research publications were collected and evaluated for experimental data on herb–drug interactions

»Herb-drug interactions are categorized into therapeutic medication classes. Drugs were categorized into therapeutic categories for accurate evaluation, and herbs with established medication interactions were chosen. Each "X" in the table denotes a single drug, and the number of "Xs" indicates the number of pharmaceuticals that interact. Drugs are grouped into their therapeutic classes in decreasing order of interactors from right to left, whereas herbs are arranged alphabetically.

Plant name	Antibiotics	Oral hypoglycemics	Anticonvulsants	Antihypertensives	NSAIDs	References
Allium sativum <b>(Garlic)</b>	xx	xx		x		(Poonam et al.2013, Rafieian Kopaei et al.2013, Al-abdeen et al.2013, Wang et al.2011, Peng et al. 2004) (Eumkeb et al.2012)
Curcuma longa <b>(Turmeric)</b>		x				(Singh et al.1995, Al Jenobi2010)
Glycyrrhiza glabra <b>(Liquorice)</b>	x					(Datla et al.1981)
Trigonella foenum-gracecum <b>(Fenugreek)</b>		xxx	x			(Alkharfy et al. 2013, Yadav et al.2010, Raju et al.1999)
Zingiber officinale <b>(Ginger)</b>		x		x		(Kshirsagar et al. 2012, Young et al.2006)
Interacting herbs	3	7	1	2	0	

**(b) Exclusion criteria decisions:**

For the initial decisions on inclusion, we excluded herbs where scientific evidence was insufficient on herb–drug interaction and/or when no observed interaction was reported.

**(c) Identification of herb–drug interactions as synergism or antagonism:**

For the 35 herbs selected, a total of 81 herb–drug interactions were identified. These interactions could be divided into synergism (a combination of herb and drug increasing pharmacological activity) and antagonism (a combination of herb and drug decreasing pharmacological activity).

**(d) Categorization of drugs in pharmacological classes:**

For accurate assessment of possibly similarly acting drugs, drugs were categorized using their

pharmacological drug class, e.g., rosiglitazone, glibenclamide, metformin, and chlor-propamide were grouped into oral hypoglycemics based on their pharmacological action and the obtained data (synergism or antagonism) was indexed. A similar table was prepared for CYP450 enzymes, another highly interacting class identified during our literature review.

»CYP450 enzyme interactions with herbs. A total of sixteen plants were found to interact with different CYP450 classes, and the same herb may have numerous interactions. For each CYP interaction, the evaluated herbal component (plant extract or phytoconstituent) is provided. Interactions could be further classified as either CYP category activation or inhibition.

Herb	Extract/phytoconstituent	CYP enzymes	Inhibition or activation	References
Allium sativum	Dipropyl sulfide, dipropyl disulfide and diallyl disulfide: dipropyl sulfide, dipropyl disulfide and diallyl disulfide	CYP2E1	Inhibition	(Kwak et al.1995, Gurley et al.2005, Siess et al. 1997, Brady et al.1991, Jin and Baillie1997, Davenport and Wargovich2005)
		CYP2B1, CYP2B2	Activation	(Siess et al.1997)
		CYP2D6, CYP3A4	No effect	(Gurley et al.2005, Markowitz2003)
		CYP1A2	No effect in healthy volunteers	(Gurley et al.2005)
		CYP1A1, CYP1A2	Activation	(Davenport and Wargovich2005)
Curcuma longa	Alcoholic extract	CYP2C9	Inhibition	(Al-Jenoobi2010, Appiah Opong et al.2007)
		CYP1A1, CYP2B1, CYP2B2, CYP2E1	Inhibition	(Oetari et al.1996)
	Curcumin	CYP1A2	Inhibition	(Appiah-Opong et al.2007, Oetari et al.1996)
		CYP2B6, CYP2D6, CYP3A4	Inhibition	(Appiah-Opong et al.2007)
Glycyrrhizin glabra	Root extract, Glycyrrhizin	CYP3A4	Activation	(Tu et al.2010, Pandit et al.2011)

#### IV. Result & Discussion:

##### Summary & Conclusions:

→DHIs are becoming more and more of a problem because of their many intricacies. Clinical trial data, both in vitro and in vivo, should be used cautiously. To prevent tragic outcomes, patient and physician education and awareness regarding DHIs in the PHC context is essential (M S, Puthiyedath R, Pillai Z S, 2025).

##### Future Directions for research & clinical practices;

→Over the past few decades, the use of herbal medications in basic care as well as the treatment of chronic and lifestyle diseases has grown significantly. Herbal medications are frequently used together with contemporary medications. All medications with a narrow therapeutic index may generally be less effective or have more side effects when used with herbal treatments. Using herbs concurrently can replicate, intensify, or counteract the effects of medications. In a small number of cases, the better understanding of herb-drug interactions has been investigated. Because negative drug interactions are frequently observed, medical professionals should advise patients not to combine herbal remedies with prescription medications. Doctors must be aware of the alleged benefits of herbal treatments since they may probably come across patients who take them. (Mehmood Z, Khan MS, Qais FA, Samreen, Ahmad I, 2019).

→We are still in the early stages of studying how medications interact with diet and herbs. Scientific research on herbal remedies is still necessary, but the knowledge gained from their long-standing traditional use should not be disregarded. It is now necessary to increase research in order to assess the efficacy and safety of herbal remedies and encourage their sensible application.

→We have demonstrated the substantial interactions between herbs used in traditional medical systems and three pharmacological classes: oral hypoglycemics, antibiotics, and anticonvulsants. The herbs *Momordica charantia*, *Terminalia bellirica*, and *Centella asiatica* showed the strongest interactions with anticonvulsants, oral hypoglycemics, and antibiotics, respectively. The most documented interactions between the medicinal herbs and CYP450 drug metabolizing enzymes were found. Furthermore, we noticed that there are no findings on antagonism in the existing literature; instead, it is exclusively based on reports on the synergistic action of herb and drug.

→Lastly, we have determined the top drug interactor categories for frequently used herbs. While this information is not definitive and may depend on the popularity of specific herbs for researching herb-drug interactions, these drug categories demonstrate the existence of herb-drug interactions that have been underreported in the literature.

##### References:

- [1]. Al-Arifi MN, Wajid S, Al-Manie NK, et al. Evaluation of knowledge of health care professionals on warfarin interactions with drug and herb medicinal in Central Saudi Arabia. *Pak J Med Sci.* 2016;32(1):229-233.
- [2]. Al-Jenoobi FI. Effects of some commonly used Saudi folk herbal medications on the metabolic activity of CYP2C9 in human liver microsomes. *Saudi Pharm J.* 2010;18(3):167-171.
- [3]. Alkharfy KM, et al. Effects of *Lepidium sativum*, *Nigella sativa* and *Trigonella foenum-graecum* on phenytoin pharmacokinetics in beagle dogs. *Phytother Res.* 2013;27(12):1800-1804.
- [4]. Appiah-Opong R, et al. Inhibition of human recombinant cytochrome P450s by curcumin and curcumin decomposition products. *Toxicology.* 2007;235(1-2):83-91.
- [5]. Asdaq SM, Inamdar MN, Asad M. Pharmacodynamic interaction of garlic with propranolol in ischemia-reperfusion induced myocardial damage. *Pak J Pharm Sci.* 2010;23(1):42-47.
- [6]. Attele AS, Wu JA, Yuan CS. Ginseng pharmacology: Multiple constituents and multiple actions. *Biochem Pharmacol.* 1999;58(11):1685-1693.
- [7]. Avula PR, Asdaq SM, Asad M. Effect of aged garlic extract and S-allyl cysteine and their interaction with atenolol during isoproterenol induced myocardial toxicity in rats. *Indian J Pharmacol.* 2014;46:94-99.
- [8]. Bordia A. Effect of garlic on human platelet aggregation in vitro. *Atherosclerosis.* 1978;30(4):355-360.
- [9]. Brady JF, et al. Modulation of rat hepatic microsomal mono-oxygenase enzymes and cytotoxicity by diallyl sulfide. *Toxicol Appl Pharmacol.* 1991;108(2):342-354.
- [10]. Budzinski JW, Foster BC, Vandenhoeck S, Arnason JT. An in vitro evaluation of human cytochrome P450 3A4 inhibition by selected commercial herbal extracts and tinctures. *Phytomedicine.* 2000;7(4):273-282.

- [11]. Butterweck V, Darenforf H, Gaus W, Narstedt A, Schulz V, Unger M. Pharmacokinetic herb-drug interactions: are preventative screenings necessary and appropriate? *Planta Med.* 2004;70:784-791.
- [12]. Chan JY, Yuen AC, Chan RY, Chan SW. A review of the cardiovascular benefits and antioxidant properties of allicin. *Phytother Res.* 2013;27:637-646.
- [13]. Chang TK, Chen J, Benetton SA. In vitro effect of standardized ginseng extracts and individual ginsenosides on the catalytic activity of human CYP1A1, CYP1A2, and CYP1B1. *Drug Metab Dispos.* 2002;30(4):378-384.
- [14]. Chen X, Hong Y, Zheng P. Efficacy and safety of extract of *Ginkgo biloba* as an adjunct therapy in chronic schizophrenia: A systematic review of randomized, double-blind, placebo-controlled studies with meta-analysis. *Psychiatry Res.* 2015;228(1):121-127.
- [15]. Christensen LP. Ginsenosides: Chemistry, biosynthesis, analysis, and potential health effects. *Adv Food Nutr Res.* 2008;55:1-99.
- [16]. Davenport DM, Wargovich MJ. Modulation of cytochrome P450 enzymes by organosulfur compounds from garlic. *Food Chem Toxicol.* 2005;43(12):1753-1762.
- [17]. Datla R, Rao SR, Murthy KJ. Excretion studies of nitrofurantoin and nitrofurantoin with deglycyrrhizinized liquorice. *Indian J Physiol Pharmacol.* 1981;25(1):59-63.
- [18]. Deferme S, Augustijns P. The effect of food components on the absorption of P-gp substrates: a review. *J Pharm Pharmacol.* 2002;55:153-162.
- [19]. DeKosky ST, Williamson JD, Fitzpatrick AL, et al. *Ginkgo biloba* for prevention of dementia: a randomized controlled trial. *JAMA.* 2008;300(19):2253-2262.
- [20]. Diamond BJ, Shiflett SC, Feiwei N, et al. *Ginkgo biloba* extract: mechanisms and clinical indications. *Arch Phys Med Rehabil.* 2000;81(5):668-678.
- [21]. Dietary Supplement Health and Education Act of 1994.
- [22]. Directive 2004/24/EC of the European Parliament and of Council of 31 March 2004.
- [23]. Dresser GK, Schwarz UI, Wilkinson GR, Kim RB. Coordinate induction of both cytochrome P4503A and MDR1 by *St John's wort* in healthy subjects. *Clin Pharmacol Ther.* 2003;73:41-50.
- [24]. Durr D, Stieger B, Kullak-Ublick GA, et al. *St John's wort* induces intestinal P-glycoprotein/MDR1 and intestinal and hepatic CYP3A4. *Clin Pharmacol Ther.* 2000;68:598-604.
- [25]. Eisenberg DM, Davis RB, Ettner SL, et al. Trends in alternative medicine use in the United States, 1990-1997: results of a follow-up national survey. *JAMA.* 1998;280:1569-1575.
- [26]. Eisenberg DM, Kessler RC, Foster C, et al. Unconventional medicine in the United States: prevalence, costs, and patterns of use. *N Engl J Med.* 1993;328:246-252.
- [27]. Ernst E. *St John's Wort* supplements endanger the success of organ transplantation. *Arch Surg.* 2002;137:316-319.
- [28]. Eumkeb G, et al. Synergistic activity and mode of action of flavonoids isolated from smaller galangal and amoxicillin combinations against amoxicillin-resistant *Escherichia coli*. *J Appl Microbiol.* 2012;112(1):55-64.
- [29]. Foster BC, Foster MS, Vandenhoeck S, et al. An in vitro evaluation of human cytochrome P450 3A4 and P-glycoprotein inhibition by garlic. *J Pharm Pharm Sci.* 2001;4(2):176-184.
- [30]. Fugh-Berman A, Ernst E. Herb-drug interactions: review and assessment of report reliability. *Br J Clin Pharmacol.* 2001;52:587-595.
- [31]. Galluzi S, Nanetti O, Binetti G, et al. Coma in a patient with Alzheimer's disease taking low-dose trazodone and *Ginkgo biloba*. *J Neurol Neurosurg Psychiatry.* 2000;68:679-683.
- [32]. Garodia P, Ichikawa H, Malani N, Sethi G, Aggarwal BB. From ancient medicine to modern medicine: ayurvedic concepts of health and their role in inflammation and cancer. *J Soc Integr Oncol.* 2007;5:25-37.
- [33]. Gorski JC, Huang SM, Pinto MD, et al. The effect of echinacea (*Echinacea purpurea* root) on cytochrome P450 activity in vivo. *Clin Pharm Ther.* 2004;75(1):89-100.
- [34]. Gurley BJ, Gardner SF, Hubbard MA, et al. Cytochrome P450 phenotypic ratios for predicting herb-drug interactions in humans. *Clin Pharm Ther.* 2002;72(3):276-287.
- [35]. Gurley BJ, et al. Clinical assessment of effects of botanical supplementation on cytochrome P450 phenotypes in the elderly: *St John's wort*, garlic oil, *Panax ginseng* and *Ginkgo biloba*. *Drugs Aging.* 2005;22(6):525-539.

- [36]. Hebert MF, Park JM, Chen YL, Akhtar S, Larson AM. Effects of St John's wort (*Hypericum perforatum*) on tacrolimus pharmacokinetics in healthy volunteers. *J Clin Pharmacol*. 2004;44(1):89-94.
- [37]. Holbrook AM, Pereira JA, Labiris R, et al. Systematic overview of warfarin and its drug and food interactions. *Arch Intern Med*. 2005;165(10):1095-1106.
- [38]. Ihl R, Bachinskaya N, Korczyn AD, et al. Efficacy and safety of a once-daily formulation of Ginkgo biloba extract EGb 761 in dementia with neuropsychiatric features: a randomized controlled trial. *Int J Geriatr Psychiatry*. 2011;26(11):1186-1194.
- [39]. Izzo AA, Ernst E. Interactions between herbal medicines and prescribed drugs: an updated systematic review. *Drugs*. 2009;69:1777-1798.
- [40]. Izzo AA, Borrelli F, Capasso R. Herbal medicine: the dangers of drug interaction. *Trends Pharmacol Sci*. 2002;23:358-359.
- [41]. Jana S, Rastogi H. Effects of caffeic acid and quercetin on in vitro permeability, metabolism and in vivo pharmacokinetics of melatonin in rats: potential for herb-drug interaction. *Eur J Drug Metab Pharmacokinet*. 2017;42(5):781-791.
- [42]. Jiang X, Sun Y, Shang L, Yang C, Kong L, Zhang Z. Green tea extract-assembled nanoclusters for combinational photothermal and chemotherapy. *J Mater Chem B*. 2019;7(39):5972-5982.
- [43]. Jin L, Baillie TA. Metabolism of the chemoprotective agent diallyl sulfide to glutathione conjugates in rats. *Chem Res Toxicol*. 1997;10(3):318-327.
- [44]. Jones BD, Runikis AM. Interaction of ginseng with phenelzine. *J Clin Psychopharmacol*. 1987;7:201-202.
- [45]. Kajiyama Y, Fujii K, Takeuchi H, Manabe Y. Ginkgo seeds poisoning. *Pediatrics*. 2002;109(2):325-327.
- [46]. Kim DS, Kim Y, Jeon JY, Kim MG. Effect of Red Ginseng on cytochrome P450 and P-glycoprotein activities in healthy volunteers. *J Ginseng Res*. 2016;40(4):375-381.
- [47]. Kiss T, Timár Z, Szabó A, et al. Effect of green tea on the gastrointestinal absorption of amoxicillin in rats. *BMC Pharmacol Toxicol*. 2019;20(1):54.
- [48]. Klishadi MS, Zarei F, Hejazian SH, et al. Losartan protects the heart against ischemia reperfusion injury: Sirtuin 3 involvement. *J Pharm Pharm Sci*. 2015;18(1):112-123.
- [49]. Kshirsagar RU, Joshi U, Biyani KR. Effect of Zingiber officinale (Linn) ethanolic extract on metformin induced hypoglycemia in alloxan induced diabetic mice. *Indian Drugs*. 2012;49:30-38.
- [50]. Kulkarni SK, George B, Mathur R. Protective effect of Withania somnifera root extract on electrographic activity in a lithium-pilocarpine model of status epilepticus. *Phytother Res*. 1998;12(6):451-453.
- [51]. Kwak MK, Kim SG, Kim ND. Effects of garlic oil on rat hepatic P4502E1 expression. *Xenobiotica*. 1995;25(10):1021-1029.
- [52]. Lawson LD, Wang ZJ. Allicin and allicin-derived garlic compounds increase breath acetone through allyl methyl sulfide: use in measuring allicin bioavailability. *J Agric Food Chem*. 2005;53(6):1974-1983.
- [53]. Lin YC, Bioteau AB, Ferrari LR, Berde CB. The use of herbs and complementary medicine in pediatric preoperative patients. *J Clin Anesth*. 2004;16(1):4-6.
- [54]. Liu Y, Zhang JW, Li W, et al. Ginsenoside metabolites, rather than naturally occurring ginsenosides, lead to inhibition of human cytochrome P450 enzymes. *Toxicol Sci*. 2006;91(2):356-364.
- [55]. Mamindla S, Prasad KVSRRG, Koganti. Herb-drug interactions: an overview of mechanisms and clinical aspects. *Int J Pharm Sci Res*. 2016;7(9):3576-3586.
- [56]. Markowitz JS, Donovan JL, DeVane CL, et al. Multiple doses of saw palmetto (*Serenoa repens*) did not alter cytochrome P450 2D6 and 3A4 activity in normal volunteers. *Clin Pharmacol Ther*. 2003;74(6):536-542.
- [57]. Markowitz JS. Effects of garlic (*Allium sativum* L.) supplementation on cytochrome P450 2D6 and 3A4 activity in healthy volunteers. *Clin Pharmacol Ther*. 2003;74(2):170-177.
- [58]. McCoubrie M. Doctors as patients: lisinopril and garlic. *Br J Gen Pract*. 1996;46:107.
- [59]. Mehmood Z, Khan MS, Qais FA, Samreen, Ahmad I. Herb and modern drug interactions: efficacy, quality, and safety aspects. In: Farooqi AA, Ismail T, editors. *New Look to Phytomedicine*. Elsevier; 2019. p. 503-520.
- [60]. Meyboodi M, Mohammadpour AH, Emami SA, Karbasforooshan H. Drug interactions of green tea. *J Pharm Care*. 2020;196-203.
- [61]. Moore LB, Goodwin B, Jones SA, et al. St John's wort induces hepatic drug metabolism

- through activation of the pregnane X receptor. *Proc Natl Acad Sci USA*. 2000;97:7500-7502.
- [62]. Morimoto T, Kotegawa T, Tsutsumi K, et al. Effect of St John's wort on the pharmacokinetics of theophylline in healthy human volunteers. *J Clin Pharmacol*. 2004;44(1):95-101.
- [63]. Odebunmi EO, Oluwaniyi OO, Bashiru MO. Comparative proximate analysis of some food condiments. *J Appl Sci Res*. 2009;2(1):1-3.
- [64]. Oetari S, et al. Effects of curcumin on cytochrome P450 and glutathione S-transferase activities in rat liver. *Biochem Pharmacol*. 1996;51(1):39-45.
- [65]. Pandit S, et al. Metabolism mediated interaction of  $\alpha$ -asarone and *Acorus calamus* with CYP3A4 and CYP2D6. *Fitoterapia*. 2011;82(3):369-374.
- [66]. Peng CC, et al. Incidence and severity of potential drug-dietary supplement interactions in primary care patients: an exploratory study of 2 outpatient practices. *Arch Intern Med*. 2004;164(6):630-636.
- [67]. Piscitelli SC, Burstein AH, Chait D, Alfaro RM, Falloon J. Indinavir concentrations and St John's wort. *Lancet*. 2000;355:547-548.
- [68]. Ponto LL, Schultz SK. Ginkgo biloba extract: review of CNS effects. *Ann Clin Psychiatry*. 2003;15:109-119.
- [69]. Poonam T, Prakash GP, Kumar LV. Influence of *Allium sativum* extract on the hypoglycemic activity of glibenclamide: an approach to possible herb-drug interaction. *Drug Metab Drug Interact*. 2013;28(4):225-230.
- [70]. Rafieian-Kopaei M, et al. Efficacy of co-administration of garlic extract and metformin for prevention of gentamicin-renal toxicity in Wistar rats: a biochemical study. *Int J Prev Med*. 2013;4(3):258-264.
- [71]. Ramanathan MR, Penzak SR. Pharmacokinetic drug interactions with Panax ginseng. *Eur J Drug Metab Pharmacokin*. 2017;42(4):545-557.
- [72]. Rao A, Karanth KS. Neuropharmacological activity of *Withania somnifera*. *Fitoterapia*. 1990;61(3):237-240.
- [73]. Reddy GD, Reddy AG, Rao GS, Kumar MV. Pharmacokinetic interaction of garlic and atorvastatin in dyslipidemic rats. *Indian J Pharmacol*. 2012;44(2):246-252.
- [74]. Resolution WHA62.13. Traditional medicine. Geneva: World Health Organization; 2009.
- [75]. Roy-Byrne PP, Bystritsky A, Russo J, Craske MG, Sherbourne CD, Stein MB. Use of herbal medicine in primary care patients with mood and anxiety disorders. *Psychosomatics*. 2005;46:117-122.
- [76]. Ruschitzka F, Meier PJ, Turina M, Luscher TF, Noll G. Acute heart transplant rejection due to Saint John's wort. *Lancet*. 2000;355:548-549.
- [77]. Shen-nung pen ts'ao ching (Divine Husbandman's Materia Medica).
- [78]. Siess MH, et al. Modification of hepatic drug-metabolizing enzymes in rats treated with alkyl sulfides. *Cancer Lett*. 1997;120(2):195-201.
- [79]. Singh A, Singh SP, Bamezai R. Postnatal modulation of hepatic biotransformation system enzymes via translactational exposure of F1 mouse pups to turmeric and curcumin. *Cancer Lett*. 1995;96(1):87-93.
- [80]. Sparreboom A, Cox MC, Acharya MR, Figg W. Herbal remedies in the United States: potential adverse interactions with anticancer agents. *J Clin Oncol*. 2004;22(12):2498-2503.
- [81]. Sugiyama T, Kubota Y, Shinozuka K, et al. Induction and recovery of hepatic drug metabolizing enzymes in rats treated with Ginkgo biloba extract. *Food Chem Toxicol*. 2004;42:953-957.
- [82]. Sugiyama T, Kubota Y, Shinozuka K, et al. Ginkgo biloba extract modifies hypoglycemic action of tolbutamide via hepatic cytochrome P450 mediated mechanism in aged rats. *Life Sci*. 2004;75(9):1113-1122.
- [83]. Sugomoto K, Ohmori M, Tsuruoka S, et al. Different effects of St John's wort on the pharmacokinetics of simvastatin and pravastatin. *Clin Pharmacol Ther*. 2001;70(6):518-524.
- [84]. Tandon SSYN. Safety reviews on selected Indian medicinal plants. New Delhi: Indian Council of Medical Research; 2018.
- [85]. Tannergreen C, Engman H, Knutson L, et al. St John's wort decreases the bioavailability of R- and S-verapamil through induction of the first-pass metabolism. *Clin Pharmacol Ther*. 2004;75(4):298-309.
- [86]. Tu JH, et al. Effect of glycyrrhizin on the activity of CYP3A enzyme in humans. *Eur J Clin Pharmacol*. 2010;66(8):805-810.
- [87]. Unger M. Pharmacokinetic drug interactions involving Ginkgo biloba. *Drug Metab Rev*. 2013;45(3):353-385.
- [88]. Walker JB. Evaluation of the ability of seven herbal resources to answer questions about

- herbal products asked in drug information centers. *Pharmacotherapy*. 2002;22:1611-1615.
- [89]. Wang EJ, Barecki-Roach M, Johnson WW. Quantitative characterization of direct P-glycoprotein inhibition by St John's wort. *J Pharm Pharmacol*. 2004;56(1):123-128.
- [90]. Wang L, Zhang Y, Wang Z, et al. Inhibitory effect of ginsenoside-Rd on carrageenan-induced inflammation in rats. *Can J Physiol Pharmacol*. 2012;90(2):229-236.
- [91]. Wang LS, Zhou G, Zhu B, et al. St John's wort induces both cytochrome P450 3A4-catalyzed sulfoxidation and 2C19-dependent hydroxylation of omeprazole. *Clin Pharmacol Ther*. 2004;75(4):191-197.
- [92]. Wang Y, et al. Effect of diallyl trisulfide on the pharmacokinetics of nifedipine in rats. *J Food Sci*. 2011;76(1):T30-T34.
- [93]. Wang Y, Choi HK, Brinckmann JA, Jiang X, Huang L. Chemical analysis of Panax quinquefolius (North American ginseng): A review. *J Chromatogr A*. 2015;1426:1-15.
- [94]. Williamson EM. Drug interactions between herbal and prescription medicines. *Drug Saf*. 2003;26(15):1075-1092.
- [95]. World Health Organization. Traditional medicine [fact sheet no. 134]. Geneva: WHO; 2003.
- [96]. Xin Y, Nan C, Chun-Hua MA, et al. Ginkgo biloba extracts attenuate lipopolysaccharide-induced inflammatory responses in acute lung injury by inhibiting the COX-2 and NF- $\kappa$ B pathways. *Chin J Nat Med*. 2015;13(1):52-58.
- [97]. Yadav M, et al. Complementary and comparative study on hypoglycemic and antihyperglycemic activity of various extracts of *Eugenia jambolana* seed, *Momordica charantia* fruits, *Gymnema sylvestre*, and *Trigonella foenum graecum* seeds in rats. *Appl Biochem Biotechnol*. 2010;160(8):2388-2400.
- [98]. Yin OQ, Tomlinson B, Waye MM, Chow AH, Chow MS. Pharmacogenetics and herb-drug interactions: experience with Ginkgo biloba and omeprazole. *Pharmacogenet Genomics*. 2004;14(12):841-850.
- [99]. Yoshioka M, Ohnishi N, Koishi T, et al. Studies on interactions between functional foods or dietary supplements and medicines. IV. Effects of Ginkgo biloba leaf extract on the pharmacokinetics and pharmacodynamics of nifedipine in healthy volunteers. *Biol Pharm Bull*. 2004;27(12):2006-2009.
- [100]. Young HY, et al. Synergistic effect of ginger and nifedipine on human platelet aggregation: a study in hypertensive patients and normal volunteers. *Am J Chin Med*. 2006;34(4):545-551.
- [101]. Yuan HD, Kim JT, Kim SH, Chung SH. Ginseng and diabetes: the evidences from in vitro, animal and human studies. *J Ginseng Res*. 2012;36(1):27-39.
- [102]. Zhou S, Chan E, Pan SQ, Huang M, Lee EJ. Pharmacokinetic interactions of drugs with St John's wort. *J Psychopharmacol*. 2004;18(2):269-283.
- [103]. Zhou S, Gao Y, Huang M, Xu A, Paxton JW. Interactions of herbs with cytochrome P450. *Drug Metab Rev*. 2003;35(1):35-98.
- [104]. Zhou S, Lim LY, Chowbay B. Herbal modulation of P-glycoprotein. *Drug Metab Rev*. 2004;36(1):1-48.
- [105]. Zhou Y, Chuan KB, Chen S. An information system model in Chinese herbal medicine manufacturing enterprises. *J Manufact Tech*. 2005;16:145-155.