

UNVEILING THE PHYTOCHEMICAL AND PHARMACOLOGICAL POTENTIAL OF HOLOPTELEA INTEGRIFOLIA SEEDS: A STUDY OF PHYTOCHEMICAL SCREENING, ANTIOXIDANT, ANTI-INFLAMMATORY AND ANTICANCER ACTIVITIES

Dr. P. Aravanan, N. Nandhini*, C. Anushka, V. Mohammed NAVAS, M. Lakshmanan, J. Ajai

Sree Abirami College of Pharmacy, Affiliated To Tamil Nadu Dr.M.G.R. Medical University, Coimbatore-21, Tamil Nadu, India.



*Corresponding Author: N. Nandhini

Sree Abirami College of Pharmacy, Affiliated To Tamil Nadu Dr.M.G.R. Medical University, Coimbatore-21, Tamil Nadu, India. DOI: <https://doi.org/10.5281/zenodo.23037146>



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ABSTRACT

Holoptelea integrifolia (Roxb.) Planch. is a traditionally used medicinal plant containing diverse phytochemicals with significant pharmacological potential. Phytochemical investigations of its leaves, bark, and twigs have identified various bioactive constituents, including alkaloids, flavonoids, tannins, saponins, phenols, terpenoids, steroids, glycosides, stigmasterol, friedelin, and other compounds. Extracts prepared using petroleum ether, ethyl acetate, ethanol, and hydroalcoholic solvents demonstrated antioxidant, antimicrobial, and antiproliferative activities. In DPPH assays, 70% ethanol extracts of leaves and bark exhibited mild antioxidant activity compared with ascorbic acid. Most tested extracts showed antimicrobial activity against bacterial and fungal strains, with bark extracts generally producing stronger inhibition than leaf extracts. Furthermore, petroleum ether and 70% ethanol bark extracts demonstrated significant antiproliferative activity against A549 lung and HeLa cervical cancer cell lines, with IC_{50} values below 20 μ g/mL. Chromatographic and spectroscopic investigations also resulted in the isolation and identification of stigmasterol, octamethylcyclohexane-1,4-dione, and di-myo-inositol, including a compound reported as a new phytochemical finding for the species. In addition, solid lipid nanoparticles (SLNs) loaded with *H. integrifolia* extract were developed to improve antifungal efficacy. The optimized formulation exhibited suitable particle characteristics, approximately 69.9% entrapment efficiency, a particle size of about 218.6 nm, and sustained drug release for 24 hours. The SLN formulation showed enhanced antifungal activity against *Candida albicans* compared with the free extract. Overall, these findings highlight the therapeutic potential of *H. integrifolia* and its extracts as sources of antimicrobial, antioxidant, anticancer, and antifungal agents.

KEYWORDS: *Holoptelea integrifolia* seeds, phytochemical screening, antioxidant, anti-inflammatory, anticancer,

INTRODUCTION

Medicinal plants represent an important reservoir of naturally occurring bioactive compounds and have been extensively used in traditional healthcare systems for the prevention and treatment of various diseases. The presence of secondary metabolites such as flavonoids, phenolic compounds, alkaloids, tannins, terpenoids, steroids, saponins, and glycosides contributes to their diverse biological activities. In recent years, increasing attention has been directed toward medicinal plants as potential sources of novel therapeutic agents, particularly

because of the limitations associated with synthetic drugs and the growing occurrence of antimicrobial resistance.

Holoptelea integrifolia (Roxb.) Planch. is a medicinally important plant belonging to the family Ulmaceae and is widely distributed throughout the Indian subcontinent.

Traditionally, different parts of this plant, including leaves, bark, roots, fruits, and seeds, have been used in the management of inflammatory conditions, gastrointestinal disorders, diabetes, skin diseases,

wounds, infections, and other ailments. The therapeutic properties of *H. integrifolia* are believed to be associated

with its rich phytochemical profile.



FIG 1: *Holoptelea integrifolia* seed.

Previous studies have reported the presence of several phytoconstituents in different extracts of *H. integrifolia* and demonstrated promising antioxidant, antimicrobial, anti-inflammatory, wound-healing, and anticancer activities. Compounds such as stigmasterol, friedelin, phenolic compounds, and other secondary metabolites have been identified from various plant parts. However, the pharmacological potential of the seeds has received comparatively less attention than the leaves, bark, and roots.

Therefore, the present investigation was undertaken to evaluate the phytochemical constituents and pharmacological potential of *H. integrifolia* seeds, with particular emphasis on antioxidant, anti-inflammatory, and anticancer activities.

The study aims to provide scientific evidence supporting the traditional medicinal importance of the plant and to explore its potential as a valuable source of naturally derived bioactive compounds.

Botanical description of *Holoptelea integrifolia*

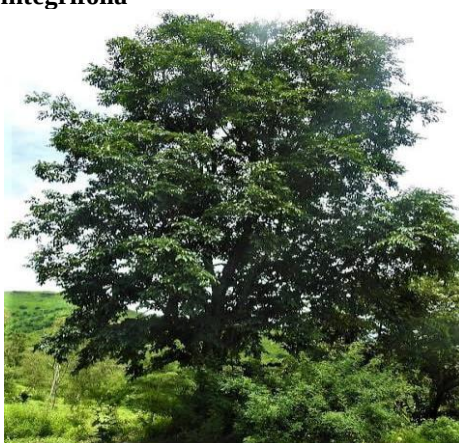


FIG 2: *Holoptelea integrifolia* tree.

1. Botanical Name

- *Holoptelea integrifolia* (Roxb.) Planch.

2. Family

- Ulmaceae – Elm family

3. Common Names

- **English:** Indian Elm, Indian Cork Tree
- **Sanskrit:** Chirabilva
- **Hindi:** Chilbil, Chilbilva

- **Tamil:** Aylai, Poothigam, Aavu, Aavi, Aiyini, Aya, Tambachi
- **Telugu:** Nemalinara, Nauli, Thapasi
- **Kannada:** Tapasi mara
- **Malayalam:** Avil
- **Ayurvedic name:** Chirabilva

Taxonomical Classification

S. No	Taxonomical Rank	Classification
1.	Kingdom	Plantae
2.	Division	Tracheophyte (Angiosperms)
3.	Class	Magnoliopsida
4.	Order	Rosales

5.	Family	Ulmaceae
6.	Genus	Holoptelea
7.	Species	<i>Holoptelea integrifolia</i> (Roxb) Planch

Common Names

Indian elm, Jungle cork tree, chirabilva



FIG 3: *Holoptelea integrifolia* BUD FIG 4: *Holoptelea integrifolia* leaves.

Phytochemical Constituents

Holoptelea integrifolia (Roxb.) Planch. contains a diverse range of primary and secondary metabolites. Phytochemical investigations of different parts of the

plant, particularly the leaves, bark, stem and seeds, have reported the presence of the following constituents.^[10,14,23,24,29,30]

Phytochemical group	Reported constituents/examples
Flavonoids	Quercetin, kaempferol and related flavonoid compounds
Phenolic compounds	Phenolic acids and other polyphenolic constituents
Tannins	Hydrolysable and condensed tannin-type compounds
Alkaloids	Alkaloidal constituents have been reported in preliminary screening
Saponins	Saponin-type constituents
Terpenoids	Various terpenoid compounds
Steroids	Steroidal constituents, including phytosterol-type compounds
Glycosides	Different glycosidic constituents
Carbohydrates	Soluble sugars and other carbohydrate constituents
Proteins and amino acids	Detected particularly in seed material
Lipids/fixed oils	Reported mainly in seeds
Phytosterols	Plant sterol constituents
Volatile constituents	Various volatile compounds have been reported from some plant parts

Pharmacological Activities of *Holoptelea integrifolia*

Holoptelea integrifolia (Roxb.) Planch. has been investigated in traditional medicine and experimental studies for several pharmacological activities. The reported activities are associated with phytoconstituents such as flavonoids, phenolic compounds, tannins, terpenoids, steroids and other secondary metabolites.

1. Antioxidant activity

Extracts of *H. integrifolia* have demonstrated antioxidant potential in experimental assays. Phenolic and flavonoid constituents may contribute to free-radical scavenging and reduction of oxidative stress.

Commonly evaluated assays include

- DPPH radical-scavenging assay
- ABTS assay
- Ferric reducing antioxidant power (FRAP) assay

- Hydrogen peroxide scavenging assay

2. Anti-inflammatory activity

Different plant extracts have shown potential to reduce inflammatory responses in experimental models. The activity may be related to inhibition of inflammatory mediators and enzymes involved in the inflammatory process.

3. Anticancer activity

Preliminary experimental investigations have reported cytotoxic or antiproliferative potential for some extracts/fractions of *H. integrifolia*. Polyphenols and other secondary metabolites may contribute to these effects. However, the evidence should be described as preclinical, and more studies are required to establish specific anticancer mechanisms.

4. Antimicrobial activity

Extracts of different parts of *H. integrifolia* have been investigated against selected bacterial and fungal species. The antimicrobial effect may be associated with phenolics, flavonoids, tannins and terpenoid constituents.

5. Antidiabetic activity

Experimental studies have investigated the plant for potential antihyperglycemic and enzyme-inhibitory effects, including inhibition of carbohydrate-digesting enzymes. Such findings suggest possible relevance to glucose metabolism, although clinical evidence is limited.

6. Antiulcer and gastroprotective activity

Traditional use and experimental investigations suggest possible gastroprotective and antiulcer properties of certain preparations of the plant.

7. Hepatoprotective activity

Some experimental studies have explored the potential of *H. integrifolia* extracts to protect liver tissue against chemically induced oxidative or toxic injury.

8. Analgesic activity

Experimental investigations have reported potential analgesic activity, which may be related to the plant's anti-inflammatory constituents.

9. Anthelmintic activity

Certain extracts have been investigated for activity against helminths, supporting some of the traditional medicinal applications of the plant.

10. Antidiarrhoeal activity

Plant extracts have also been investigated for antidiarrhoeal effects in experimental models, potentially through effects on intestinal motility and secretion.

Mechanism of Action of *Holoptelea integrifolia*

The pharmacological effects of *Holoptelea integrifolia* are thought to arise from its phenolic compounds, flavonoids, tannins, terpenoids, steroids and other secondary metabolites. The proposed mechanisms vary according to the activity and require further experimental confirmation.

1. Antioxidant mechanism

Flavonoids and phenolic compounds may

The antioxidant activity may be attributed to the ability of phytoconstituents to scavenge free radicals such as DPPH and other reactive oxygen species (ROS). These compounds can donate hydrogen atoms or electrons to unstable free radicals, thereby neutralizing them and reducing oxidative damage to cellular lipids, proteins, and DNA. Furthermore, they may enhance endogenous antioxidant defenses, including superoxide dismutase (SOD), catalase (CAT), and glutathione (GSH), helping to protect cells against oxidative stress.

Proposed pathway

Plant phenolics/flavonoids → free-radical scavenging + antioxidant defense → ↓ oxidative stress.

2. Anti-inflammatory mechanism

The anti-inflammatory activity may involve suppression of inflammatory mediators and signaling pathways.

The anti-inflammatory activity may involve inhibition of the cyclooxygenase (COX) and lipoxygenase (LOX) pathways, thereby reducing the production of inflammatory mediators such as prostaglandins and leukotrienes. The phytoconstituents may also suppress the release of pro-inflammatory cytokines, including TNF- α , IL-1 β , and IL-6. Furthermore, modulation of NF- κ B and related inflammatory signaling pathways may help reduce inflammatory responses and tissue damage.

Proposed pathway

Bioactive constituents → ↓ NF- κ B/inflammatory signaling → ↓ cytokines and inflammatory mediators → ↓ inflammation.

3. Anticancer mechanism

For anticancer activity, experimental evidence is still comparatively limited. Possible mechanisms of plant-derived constituents include:

The anticancer activity may involve multiple mechanisms, including inhibition of cancer-cell proliferation and induction of programmed cell death (apoptosis). Bioactive constituents may alter mitochondrial membrane function and activate caspases involved in apoptotic pathways. They may also regulate the cell cycle, thereby limiting uncontrolled cell division. In addition, reduction of oxidative stress and modulation of pro-survival signaling pathways may contribute to the suppression of cancer-cell growth and survival.

Proposed pathway

Bioactive compounds → cell-cycle modulation/apoptotic signaling → ↓ cancer-cell proliferation.

4. Antimicrobial mechanism

Phenolic compounds, tannins, and terpenoids may contribute to the antimicrobial activity by disrupting microbial cell membranes and altering membrane permeability. These phytochemicals can also interfere with essential microbial enzymes and proteins, thereby affecting normal cellular functions. In addition, phenolic compounds may inhibit microbial growth and multiplication, contributing to the overall antimicrobial potential of the plant extract.

5. Antidiabetic mechanism

Compounds such as tannins, terpenoids, and phenolic compounds may exhibit antimicrobial activity by disrupting microbial cell membranes, altering membrane permeability, and interfering with microbial enzymes and

proteins. These effects can inhibit microbial growth and multiplication.

Some constituents may also contribute to antidiabetic activity by inhibiting α -amylase and α -glucosidase, thereby reducing carbohydrate breakdown and delaying glucose absorption. In addition, their antioxidant properties may provide protection against oxidative stress associated with diabetes.

Proposed pathway

Extract/active constituents $\rightarrow$ enzyme inhibition $\rightarrow$ $\downarrow$ carbohydrate digestion $\rightarrow$ $\downarrow$ postprandial glucose absorption.

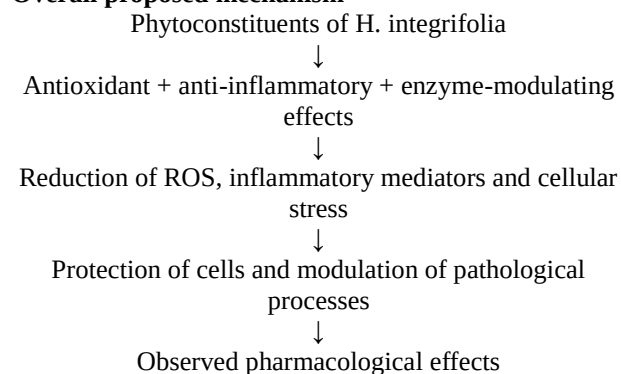
6. Hepatoprotective mechanism

The hepatoprotective effects may be attributed to several mechanisms, including the reduction of lipid peroxidation and scavenging of reactive oxygen species (ROS). The phytoconstituents may also enhance endogenous antioxidant enzyme activity, thereby strengthening the body's defense against oxidative stress. Additionally, they may protect hepatocyte membranes from oxidative and toxic injury, contributing to the maintenance of normal liver function.

7. Analgesic mechanism

The analgesic effect may be secondary to suppression of inflammatory mediators, particularly prostaglandin-related pathways, thereby reducing peripheral inflammatory pain.

Overall proposed mechanism



Toxicity and Safety Profile

Holoptelea integrifolia (Roxb.) Planch. has a long history of traditional medicinal use, and several experimental studies have investigated the safety of its extracts. However, traditional use does not by itself establish clinical safety, and toxicity can vary according to the plant part, extraction solvent, dose and duration of administration.

1. Acute toxicity

Acute toxicity studies of selected *H. integrifolia* extracts have generally suggested low acute toxicity at experimentally tested doses. No major toxic manifestations have been reported in some animal

studies at the investigated doses. Nevertheless, safety should be interpreted only within the dose ranges actually studied.

2. Subacute and chronic toxicity

Compared with acute toxicity, long-term toxicity data are limited. Repeated-dose studies are important to evaluate possible effects on:

- Liver
- Kidney
- Blood and hematological parameters
- Body weight and general behavior
- Major biochemical parameters

More systematic chronic toxicity studies are required before establishing long-term safety.

3. Organ toxicity

Because the liver and kidneys are major organs involved in metabolism and elimination, biochemical markers such as ALT, AST, ALP, bilirubin, urea and creatinine can be monitored during toxicity studies. Histopathological examination of major organs provides additional evidence of tissue-level safety.

4. Genotoxicity and reproductive safety

There is comparatively limited information regarding the genotoxic, reproductive and developmental toxicity of *H. integrifolia*. Therefore, these aspects should be investigated before considering prolonged therapeutic use or development of standardized preparations.

5. Dose-dependent effects

The biological effects of plant extracts are often dose-dependent. A dose that produces a pharmacological effect may differ substantially from a dose that produces toxicity. Therefore, standardized extracts and clearly defined doses are essential for safety evaluation.

6. Factors affecting safety

- The safety profile may vary depending on:
- Plant part used (leaf, bark, seed, root, etc.)
- Extraction solvent
- Extraction method
- Geographical origin
- Phytochemical composition
- Dose and duration of administration
- Individual susceptibility
- *integrifolia*

Research Gaps and future perspectives

- Limited phytochemical characterization
- Many studies report broad phytochemical groups such as flavonoids, phenolics, tannins and terpenoids, but comprehensive identification and quantification of individual bioactive compounds remain limited.

- **Lack of standardized extracts**

Differences in plant part, geographical origin, extraction solvent and extraction procedure can produce different phytochemical profiles. Standardized extraction and quality-control methods are therefore required.

- **Limited mechanism-based studies**

Although antioxidant, anti-inflammatory and other pharmacological activities have been reported, the precise molecular mechanisms and signaling pathways responsible for these effects require further investigation.

- **Insufficient studies on seeds**

Compared with commonly investigated parts such as leaves and bark, the seeds of *H. integrifolia* require greater attention for detailed phytochemical and pharmacological evaluation.

- **Limited anticancer evidence**

The anticancer potential requires further investigation using well-characterized extracts, purified compounds and validated cancer models. Studies should also determine selectivity toward cancer cells versus normal cells.

- **Insufficient toxicity data**

Comprehensive acute, subacute, chronic, genotoxicity and reproductive-toxicity studies are needed to establish the safety profile of different extracts.

- **Limited pharmacokinetic information**

Data regarding absorption, distribution, metabolism, elimination and bioavailability of important constituents are scarce.

- **Lack of clinical studies**

Much of the available evidence is based on in-vitro and animal experiments. Properly designed clinical studies are required to establish efficacy and safety in humans.

Future Perspectives

Future research on *H. integrifolia* should focus on bioassay-guided fractionation and advanced analytical techniques, such as HPLC, LC-MS/MS, GC-MS and NMR, to identify and quantify bioactive compounds.

The development of standardized extracts with defined chemical markers could improve reproducibility between studies. Molecular investigations involving oxidative-stress pathways, inflammatory signaling, apoptosis and cell-cycle regulation may help clarify the pharmacological mechanisms.

For anticancer research, future studies could evaluate

- Cytotoxicity against different cancer cell lines
- Selectivity toward normal cells
- Apoptosis and cell-cycle pathways
- Molecular targets and signaling pathways
- In-vivo efficacy
- Pharmacokinetic and toxicity profiles

Nanotechnology and advanced drug-delivery systems may also be explored to improve the solubility, stability, bioavailability and targeted delivery of promising phytoconstituents.

CONCLUSION

Holoptelea integrifolia (Roxb.) Planch. is an important medicinal plant belonging to the family Ulmaceae and has been traditionally used for various therapeutic purposes. Phytochemical investigations have revealed the presence of bioactive constituents such as flavonoids, phenolic compounds, tannins, terpenoids, steroids and other secondary metabolites, which may contribute to its diverse pharmacological properties. Experimental studies have reported promising antioxidant, anti-inflammatory, antimicrobial, antidiabetic, hepatoprotective, analgesic, antiulcer and anticancer activities. In particular, its antioxidant and anti-inflammatory potential may be associated with its phenolic and flavonoid constituents. However, much of the available evidence is based on in-vitro and preclinical studies, while comprehensive information regarding the precise molecular mechanisms, standardized phytochemical profiles, pharmacokinetics, long-term toxicity and clinical efficacy remains limited. Therefore, further research involving isolation and characterization of active compounds, standardized extracts, mechanism-based investigations, comprehensive safety evaluation and well-designed clinical studies is required. Overall, *Holoptelea integrifolia* represents a promising source of pharmacologically active phytoconstituents and may have potential for future development of scientifically validated herbal therapeutic agents.

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Conflict of Interest

The authors declare that there are no conflicts of interest regarding the publication of this review article. No financial, personal, commercial, or professional interests have influenced the preparation, interpretation, or presentation of the information included in this manuscript. All authors have reviewed and approved the final manuscript and agree with its submission for publication.

REFERENCES

1. Kirtikar KR, Basu BD. Indian Medicinal Plants. 2nd ed. Dehradun: International Book Distributors; 2005.

2. Nadkarni KM. Indian Materia Medica. Mumbai: Popular Prakashan; 2009.
3. Khare CP. Indian Medicinal Plants: An Illustrated Dictionary. New York: Springer; 2007.
4. Warriar PK, Nambiar VPK, Ramankutty C. Indian Medicinal Plants: A Compendium of 500 Species. Chennai: Orient Longman; 1995.
5. Chopra RN, Nayar SL, Chopra IC. Glossary of Indian Medicinal Plants. New Delhi: Council of Scientific and Industrial Research; 1956.
6. Anonymous. The Ayurvedic Pharmacopoeia of India. New Delhi: Ministry of Health and Family Welfare, Government of India.
7. The Wealth of India. Raw Materials. Vol. 5. New Delhi: Council of Scientific and Industrial Research; 2003.
8. Nadkarni AK. Dr. K.M. Nadkarni's Indian Materia Medica. Mumbai: Popular Prakashan; 1976.
9. Pullaiah T. Encyclopedia of World Medicinal Plants. New Delhi: Regency Publications; 2006.
10. Harborne JB. Phytochemical Methods: A Guide to Modern Techniques of Plant Analysis. 3rd ed. London: Chapman & Hall; 1998.
11. Trease GE, Evans WC. Pharmacognosy. 15th ed. London: Saunders; 2002.
12. Sofowora A. Medicinal Plants and Traditional Medicine in Africa. 2nd ed. Ibadan: Spectrum Books; 1993.
13. Evans WC. Trease and Evans Pharmacognosy. 16th ed. Edinburgh: Saunders Elsevier; 2009.
14. Kokate CK, Purohit AP, Gokhale SB. Pharmacognosy. 54th ed. Pune: Nirali Prakashan; 2017.
15. Singleton VL, Orthofer R, Lamuela-Raventós RM. Analysis of total phenols and other oxidation substrates and antioxidants by means of Folin-Ciocalteu reagent. Methods Enzymol. 1999; 299: 152-178.
16. Blois MS. Antioxidant determinations by the use of a stable free radical. Nature. 1958; 181: 1199-1200.
17. Benzie IFF, Strain JJ. The ferric reducing ability of plasma (FRAP) as a measure of antioxidant power: the FRAP assay. Anal Biochem. 1996; 239(1): 70-76.
18. Brand-Williams W, Cuvelier ME, Berset C. Use of a free radical method to evaluate antioxidant activity. Lebensm Wiss Technol. 1995; 28(1): 25-30.
19. Mosmann T. Rapid colorimetric assay for cellular growth and survival: application to proliferation and cytotoxicity assays. J Immunol Methods. 1983; 65(1-2): 55-63.
20. Skehan P, Storeng R, Scudiero D, Monks A, McMahon J, Vistica D, et al. New colorimetric cytotoxicity assay for anticancer-drug screening. J Natl Cancer Inst. 1990; 82(13): 1107-1112.
21. Winter CA, Risley EA, Nuss GW. Carrageenin-induced edema in hind paw of the rat as an assay for anti-inflammatory drugs. Proc Soc Exp Biol Med. 1962; 111: 544-547.
22. Chandra S, Dave R. In vitro models for antioxidant and anti-inflammatory activity evaluation of medicinal plants. J Pharm Sci Res. 2009; 1(2): 1-8.
23. Kumar S, Pandey AK. Chemistry and biological activities of flavonoids: an overview. Sci World J. 2013; 2013: 162750.
24. Pietta PG. Flavonoids as antioxidants. J Nat Prod. 2000; 63(7): 1035-1042.
25. Reuter S, Gupta SC, Chaturvedi MM, Aggarwal BB. Oxidative stress, inflammation, and cancer: how are they linked? Free Radic Biol Med. 2010; 49(11): 1603-1616.
26. Karin M, Greten FR. NF- κ B: linking inflammation and immunity to cancer development and progression. Nat Rev Immunol. 2005; 5(10): 749-759.
27. Serhan CN, Savill J. Resolution of inflammation: the beginning programs the end. Nat Immunol. 2005; 6(12): 1191-1197.
28. Aggarwal BB, Shishodia S. Molecular targets of dietary agents for prevention and therapy of cancer. Biochem Pharmacol. 2006; 71(10): 1397-1421.
29. Atanasov AG, Waltenberger B, Pferschy-Wenzig EM, Linder T, Wawrosch C, Uhrin P, et al. Discovery and resupply of pharmacologically active plant-derived natural products: a review. Biotechnol Adv. 2015; 33(8): 1582-1614.
30. Cragg GM, Newman DJ. Natural products: a continuing source of novel drug leads. Biochim Biophys Acta. 2013; 1830(6): 3670-3695.
31. Heinrich M, Barnes J, Gibbons S, Williamson EM. Fundamentals of Pharmacognosy and Phytotherapy. 2nd ed. Edinburgh: Churchill Livingstone Elsevier; 2012.
32. World Health Organization. WHO Guidelines on Safety Monitoring of Herbal Medicines in Pharmacovigilance Systems. Geneva: World Health Organization; 2004.
33. World Health Organization. WHO Guidelines for Assessing Quality of Herbal Medicines with Reference to Contaminants and Residues. Geneva: World Health Organization; 2007.
34. OECD. Test No. 423: Acute Oral Toxicity—Acute Toxic Class Method. Paris: Organisation for Economic Co-operation and Development; 2002.
35. OECD. Test No. 407: Repeated Dose 28-Day Oral Toxicity Study in Rodents. Paris: Organisation for Economic Co-operation and Development; 2008.