



INTERNATIONAL JOURNAL OF RESEARCH IN PHARMACEUTICAL SCIENCES

Published by JK Welfare & Pharmascope Foundation

Journal Home Page: <https://ijrps.com>

Impact of herbal drugs and its clinical application

Vetriselvan Subramaniyan*¹, Saminathan Kayarohanam², Ashok Kumar J³, Vinoth Kumarasamy⁴¹Department of Pharmacology, Faculty of Medicine, MAHSA University, Malaysia²Department of Pharmacology, Geomatika University College, Malaysia³Faculty of Pharmaceutical Sciences, UCSI University, Kuala Lumpur, Malaysia⁴Department of Microbiology, Faculty of Medicine, MAHSA University, Malaysia

Article History:

Received on: 21.12.2018

Revised on: 16.02.2019

Accepted on: 19.02.2019

Keywords:

Herbal drugs,
Human health,
Drug formulation,
Adverse effects

ABSTRACT

Since ancient times until now exploring the importance of herbal medicines to treat the variety of diseases. Currently the herbal medicines searching for health, wellness and aim to achieve effective treatment without much side effect. Recent days the impact of herbal medicines well established even herbal treatment is one of the alternative medicines for most of the diseases such as hyperlipidemia, diabetes mellitus etc. Medicinal plants always have been rich sources of bioactive compounds, and that will be very helpful to human health. The reasons for herbal medicines attracted by the health care professionals and common individuals, including concern about confidence and safety of drugs. Allopathic medicines have many side effects and sometimes failing to treat and most of the herbal drugs proven better therapeutic effects without any major adverse effects. With the demand for phytomedicine user, this review highlights modern herbal drug formulation and its clinical use.



* Corresponding Author

Name: Vetriselvan Subramaniyan

Email: vetricology@gmail.com

ISSN: 0975-7538

DOI: <https://doi.org/10.26452/ijrps.v10i2.537>

Production and Hosted by

IJRPS | <https://ijrps.com>

© 2019 | All rights reserved.

INTRODUCTION

The recognition of the herbal drugs day to day increasing and arriving new formulations in the market. A number of the pharmaceutical industry to introduce herbal products because of public demand and safety of the therapy. The rational use of herbal medicine is very limited adverse effects and traditionally practicing since long years ago to treat disease, but there is no documented evidence. In this regard, recent years documenting many of the herbal drugs with scientific support (Chikezie and Ojiako, 2015; Vetriselvan *et al.*, 2018). Many documented evidence of Indian system of medicines such as Siddha and traditional medicines of Unani

and Ayurvedic. The caution of herbal medicines is very important and if using inappropriately to cause serious health issues even lethal. While the use of herbal medicines needs more documentary evidence and should be nontoxic with minimal or no side effects. Some of the herbal drugs having a more poisonous effect, then a beneficial effect. One of the global issues is poor quality due to contamination of heavy metals and poisonous substances (Ernst, 2005). Moreover, it needs proper guidelines to investigate the herbal medicines.

This is very helpful to treat multiple disease conditions without harming effects. Hundreds of polyherbal formulations are available in the market for the management of different disease conditions such as metabolic diseases and dermatological infections. Majority of formulations is more than eight drug combination, the main issues are arising from the standardization of drugs and quality. So need further investigations on quality control. The direction of food and drug administration suggests that the polyherbal formulation should be less than three drugs (Rao, 2000). The herbal system of treatment is very broad and influence their action of a variety of disease conditions including anti-hyperlipidemia and cardiac protection. Due to the

poor absorption of plant-based products, the researchers are developing new formulation and approach numerous methods to overcome the issue of rapid metabolism and systemic elimination. Moreover, the plant drug of biologically active constituents mostly soluble in water.

The plant drug molecules are a large size and can't easily be absorbed by passive diffusion, and this has low lipid solubility. The newer formulation of plant drugs aims to achieve rich penetration of biomembrane (Yang *et al.*, 2008). However, developing new drug formulations of pharmaceutical research able to solve the scientific needs, including absorption, distribution, metabolism, binding of receptor sites, mechanism of action and appropriate dosage form. Herbal drugs merging with a novel drug delivery system and to improve their systemic action. The novel system incorporated such as nanoparticles, matrix system, liposomes and microemulsions etc.. Additionally, the improvement of herbal drug formulations mainly focuses on regulatory measures and quality control as follows many countries of the world. It is envisaged that the practice of herbal medicines will be integrated into other conventional methods. Traditional intake of herbal medicines is not suitable and outdated. If applying a novel drug delivery system that may help in increasing therapeutic efficacy and reduce the unwanted side effects.

The basic idea of a novel drug delivery system to reach good manufacturing practice standards with the help of quality assurance of herbal formulations and this ensured by ingredients of herbal formulations (Kusum *et al.*, 2010). Some herbal products have a very small amount of active phytoconstituents when compared to other ingredients, several analytical techniques using herbal drug formulations to identify the constituents and to isolate product specifications. Additionally, the manufacturer should be monitor stability and shelf life of herbal products. This is very helpful for the dosage forms such as tablets, capsule preparations.

Novel approaches and its applications

Currently, various drug delivery and targeting system under development and should improve the system. It will be minimized loss of drug degradation, reduce side effects, improve the bioavailability of drug and this can help to reach the targeted sites. The component of drug carriers, one can name soluble polymers, microparticles made of insoluble or biodegradable natural and synthetic polymers, microcapsules, cells, cell ghosts, lipoproteins, liposomes, and micelles. The specific targeting of receptors and antibodies very interesting and this can be influenced by the factors of degradation of drugs, pH and temperature –sensitive.

There are two types of drug targeting system desired sites for drug release such as passive and active targeting. This is direct targeting of drug loaded system at the site of action.

Treatment with cancer therapy, need for enough vascular permeability of tissues compared with normal tissues. Passive targeting is ideal for the chemotherapeutic agents. A function of drug movements selectively targeting to the receptor sites on the surface of the cells. Also, can improve the novel system of a herbal formulation to achieve ligand-receptor interactions are highly selective and this can be more precise in the site of action. The plant extract of danshen (*Radix Salvia miltiorrhiza*) was developed with Chitosan-gelatin as a sustained release implant and showed an anastomosing healing effect of tissue and muscles (Zhao *et al.*, 2002). Previous studies reported that the marketed formulation of Aethri Blend-SR herbal extracts and nutrient supplements to support connective tissues and healthy joints in the human body.

It is clinically validated for the supportive treatment of joint care application. The blend of a natural substance contains different phytoconstituents such as baseline (a constituent of the *Boswellia serrate* extract), Glucosamine sulfate, curcumin C3 complex (phytoconstituent of *Curcuma longa*) and these ingredients synergistically to support against inflammatory diseases such as arthritis. The traditional system of Chinese medicine, practicing nanoparticles used to treat thrombus condition and thus attenuate the effect against diminution of thrombi and arterial embolism. The medicinal herbs, including of peach seed, safflower, Angelica root, Szechwan lovage rhizome, Rehmannia root, red peony root, leech, gadfly, earthworm and ground beetle. The traditional system of Chinese medicine has potential action and intensified than their non-nanoparticle (Shen *et al.*, 2008).

Nano drugs carry their herbal remedies to target diseased area and cross all the obstacles related to drug delivery due to small size easily penetrate and increased surface area (Sharma *et al.*, 2011; Chung *et al.*, 2001). One of the drug delivery systems through the skin, some of the transdermal films containing phytoconstituents of Curcuma and boswellic acid, these systems of the route of administration avoids the first-pass metabolism of drugs without pain. If offer systemic level therapy via zero-order kinetics and treatment can be easily terminated at any time. A condition of platelet agglutination and cardiomyopathy reduces with the treatment of herbal mixture Danshensu (*Salvia miltiorrhiza* Bge), Tanshinone IIA, matrine (*Sophora flavescens* Ait), puerarin (*Pueraria lobata* Phwi), oxymatrine (*Radix sophorae Flavescents*). Recent days herbal pills available in the market to

treat coronary heart disease (CHD) and this available china, the treatment effect basically similar that Isordil and there is no significant difference between them (Rakesh and Arunporn, 2017). Capsaicin and glycyrrhetic acid, a major constituent of chilies and licorice, was found that the topical administration to have local obesity effect. It showed that a significant reduction of fat thickness when administered topically (Armanini *et al.*, 2005).

Herbal lipid base delivery

There are different synthetic compounds are used for drug formulation and prone to have adverse effects. The human body will reject certain chemical compounds because some chemicals are not naturally occurring. Administration of wrong dose may tend to have severe side effects, some as mild side effects and others as severe may chance to have lethal. This incidence is very rare, and there is no frequent evidence of herbal drugs. It is important that phytomedicine produce fewer side effects and there are no unwanted effects on human body systems. Furthermore, many of the Phyto compounds standardized and incorporate them into the advanced drug delivery system (Norman, 2007).

Previous research studies investigated that lipid-based drug delivery system shown their potential targeted drug action. Pharmacosomes are amphiphilic phospholipid complexes of drugs bearing active hydrogen that bind to phospholipids. The modern phytopharmaceutical preparations are better results showed towards the bioavailability and targeting sites. Origin of phytosomes is like *Silybum Marianum* and *Ginkgo Biloba*, *ginseng* and this useful for novel preparations of drugs. Advanced formulations have high lipophilicity and therapeutic properties. Improvement of phytopharmaceutical preparations that improved pharmacokinetic parameter and effect of pharmacological responses. This method easy to treat metabolic diseases, acute liver diseases, and some infectious disease. Importantly, phytosomes develops effective action as a bridge between a novel drug delivery system and a conventional drug delivery system (Semalty *et al.*, 2009).

Regulatory control of herbal medicines

The emergence of herbal products needs for proper regulatory control and to avoid the lack of consistent terminology. Some of the herbal products classified as food products and dietary supplements. Therefore, the need to identify the classification of herbal drugs and use of targeted treatment. In the United States provides Dietary supplement act 1994 (DSHEA) sufficient information about herbal medicines. World Health Organization (WHO) has conducted a global survey on the

regulatory control of herbal medicines and has reported findings from 141 countries. This survey confirms that many countries established herbal drugs regulation during the past few years. The process of regulatory control, establishing herbal medicines national policy. The regulatory status is most important to access the herbal medicines, assessment of safety and efficacy. Additionally, in response to requests from member states, WHO has announced to provide all the essential support such as herbal drug development methodology, ensure product safety, preparation guidelines and information exchange about herbal drugs. Recent years, WHO guidelines have developed in several important areas including Pharmacovigilance, consumer information and good agricultural and collection practices (GACP) (WHO Guidelines, 2004).

In order, several countries following herbal regulatory body such as Traditional Herbal Medicinal Products Directive (THMPD) Europe, which became effective in early 2011, Traditional Chinese Medicine (TCM), since 2004, GMP standards in India, Africa, and Brazil are ongoing. These reviews concluded that regulation of herbal drugs could able to monitor the preparation of herbal products and its clinical importance. Herbal medicinal products can offer an alternative to conventional medicines in non-life-threatening conditions, providing they are of adequate quality and safety and are used in an appropriate manner (Zhou *et al.*, 2005).

Importance of herbal medicine in diabetes

Numerous published researches reported that polysaccharides from plant source normally, have excellent antidiabetic activities (Lee *et al.*, 2010). *Adina cordifolia* (Roxb) leaves contain flavonoids, phenolic compounds, tannins, saponins, and gums, etc. These ingredients are responsible for restoring the function of pancreatic tissues to increase the insulin secretion and also contribute to inhibiting the glucose absorption in the intestine. The young coconut (*Cocos nucifera* Linn) fiber, oil, juice, and flour reported being a hypoglycemic activity (Trinidad *et al.*, 2003). The presence of flavonoids is responsible for to bioactive antidiabetic activity. An anti-hypoglycemic activity of *Cocos nucifera* Linn may be enhancing the insulin action of plasma by accelerating either the pancreatic production of insulin from the beta cell or discharge from the bound insulin (29). *Anthocleista djalensis* extracts Inhibit α -amylase activity and reduced fasting blood glucose to exhibit the management of hyperglycemia (Sagar *et al.*, 2011).

Fructooligosaccharide (FOS) increase the population of Lactobacilli and Bifidobacteria, to protect the intestinal and 2 week's intake of FOS to decrease blood glucose, low-density lipoprotein and increase the body weight (Sudhanshu *et al.*, 2013).

FOS further study of molecular docking of three sugars as PPAR-c agonists and DPP-IV inhibitors and it's preferred to interact with tyrosine residues during binding to the active sites of proteins (Suba *et al.*, 2004). Methanolic leaf extract of *Axonopus compressus* reduces blood sugar levels, and this plant contain active ingredients known as flavonoids, glycosides, tannins, etc. are responsible for the antidiabetic activity (Ogie *et al.*, 2010). As per the previous study from Niles *et al.* the anti-diabetic effects of medicinal plants produced by refurbishing the function of pancreatic cells by or reduce the intestinal absorption of glucose (Kothandam *et al.*, 2012). The two new flavones isolated from *Callistemon lanceolatus* reduce the blood glucose through the reconstruction of pancreatic islets and probably stimulate insulin secretion in streptozotocin-induced *diabetic rats* (Kiruthika *et al.*, 2013).

Herbal drugs in cancer therapy

Natural source of the drug is important to treat cancer with the innovative structure and have a unique mechanism to minimize cell proliferation. Zea mays Leaf extract promotes the index level of the apoptosis process and a big impact on cell viability, nuclear fragmentation and morphological change (Buk *et al.*, 2014; Shivananjappa and Joshi, 2012). Polyphenols and flavonoids, found in *Polygonum tinctorium* Lour. Which is exhibit effective in vitro cytotoxicity against human renal cell line at the same time it was found to be safer in the normal cell (Kumar *et al.*, 2011). This effect is due to the polyphenols, and antioxidant activity of the plant confirmed through relatively between the antioxidant effects with the survival of cancer cells (Rahman *et al.*, 2013). *Leea indica* leaf extracts contain phenolic compounds like gallic acid and other antioxidant agents responsible for producing the morphological changes of inhibition in prostate cancer cell lines (Aisha *et al.*, 2015). Polyphenolic content of *Euphorbia royleana* persists the tumor inhibition based on the dose-dependent proved through the Potato disc assay (Sharvil *et al.*, 2015). The dry powdered extract of *Curcuma longa* L. (Zingiberaceae) has a major active compound known as curcumin, and these compounds exhibit the various pharmacological activities including antioxidant, anti-inflammatory, hypoglycemic, antimicrobial, lipid-lowering and hepatoprotective (Sudip *et al.*, 2005). The novel curcumin effective as a chemosensitizer and also poses the radiosensitizer on cytotoxic activities in lung squamous cell carcinoma. This curcumin effect may be the document pharmacological effect of through inhibits the cell cycle pathway apoptosis cancer cell, inhibit the proliferation and interference with inflammation, angiogenesis and invasion (Lao *et al.*, 2006). Moreover, the curcumin was documented to be

safe at a high dose of 12,000 mg /day and exhibit the accountably effective against the carcinoma (Gupta *et al.*, 2014). Brassicaceae plants containing Isothiocyanates possess the effective chemopreventive and anticancer activities this probable mechanism is associated with modulation of enzyme activities with a considerable reduction in the cancer cell cycle through induced the apoptosis of the cancer cell in different cells, at the same time this also effective reduction in angiogenesis and the metaseres (Wu *et al.*, 2009).

Centella asiatica (L) contains active chemical compounds known as triterpene centellasaponin, asiaticoside, madecassoside and civilized, responsible for the cytotoxic activity of fibroblast cells and increase the apoptosis of cancer cell into exhibit cytotoxic activity (Bonfill *et al.*, 2006).

CONCLUSION

The study revealed that the use of herbal medicine increasing worldwide. Also needs to be ascertained by further studies, including safety, drug mechanism and formulation of dosage forms. Moreover, the health care provider should also show enough commitment towards understanding the use of herbal medicines and there is a need to develop Pharmacovigilance programs.

Conflict of interest statement

No conflicts of interest.

REFERENCES

- Aisha Ashraf, Raja Adil Sarfraz, Muhammad Abid Rashid, Muhammad Shahid. Antioxidant, antimicrobial, antitumor, and cytotoxic activities of an important medicinal plant (*Euphorbia royleana*) from Pakistan. *Journal of food and drug analysis* 2015; 23: 109 e115.
- Armanini D, Nacamulli D, Francini-Pesenti F, Battagin G, Ragazzi E, Fiore C. Glycyrrhetic acid, the active principle of licorice, can reduce the thickness of subcutaneous thigh fat through topical application. *Steroids* 2005; 70(8):538-542.
- Bonfill M, Mangas S, Cusidó RM, Osuna L, Piñol MT; Palazón J. Identification of triterpenoid compounds of *Centella Asiatica* by thin-layer chromatography and mass spectrometry. *Biom. Chromatogr* 2006; 20: 151-53.
- Buk-Gu Heoa, Yun-Jum Parkb, Yong-Seo Parkc, Jong-Hyang Baeb, Ja-Yong Chod, Kun Parke, Zenon Jastrzebskif, Shela Gorinsteing. Anticancer and antioxidant effects of extracts from different parts of the indigo plant. *Industrial Crops and Products* 2014; 56: 9-16.

- Chikezie PC, Ojiako OA. Herbal Medicine: Yesterday, Today and Tomorrow. *Altern Integr Med* 2015; 4: 195.
- Chung H, Burk H, Shu K. Herbal-based oral composition and process for producing the same. 2001 European Patent EP0862446.
- Ernst E. Contamination of herbal medicines. *Pharm J* 2005; 275: 167–168.
- Gupta P, Kim B, Kim SH, Srivastava SK. Molecular targets of isothiocyanates in cancer: recent advances. *Mol. Nutr. Food Res* 2014; 58: 1685–1707.
- Kiruthika Balasubramanian, Palghat Raghunathan Padma. Anticancer Activity of Zea mays Leaf Extracts on Oxidative Stress-induced Hep2 Cells. *J Acupunct Meridian Stud* 2013; 6(3):149e158.
- Kothandam Hariprasath, Paturi Umamaheswari, Samuel David Wicket. Hormone-based therapy in type 2 diabetes mellitus. *Asian Journal of Pharmaceutical and Clinical Research* 2012; 5 (4): 20-24.
- Kumar RS, Rajkapoor B, Perumal P. In vitro and in vivo anticancer activity of Indigofera cassioides Rottl. *Ex. DC. Asian Pac. J Trop Med* 2011; 4: 379–385.
- Kusum Devi V, Nimisha Jain, Kusum Valli S. Importance of novel drug delivery systems in herbal medicines. *Pharmacogn Rev* 2010; 4(7): 27–31.
- Lao C, Ruffin M, Normolle D, Heath D, Murray S, Bailey J, Boggs M, Crowell J, Rock C, Brenner D. Dose escalation of a curcuminoid formulation. *BMC Complement. Altern Med* 2006; 6: 1–4.
- Lee BR, Lee YP, Kim DW, Song HY, Yoo KY, Won MH, Kang TC, Lee KJ, Kim KH, Joo JH, Ham HJ, Hur JH, Cho SW, Han KH, Lee KS, Park J, Eum WS, Choi SY. Amelioration of streptozotocin-induced diabetes by Agrocybe chaxingu polysaccharide. *Mol Cells* 2010; 29(4):349-54.
- Norman GB. A Handbook for Practice on a Scientific Basis. 2nd ed. New York: Medpharm Scientific Publishers, Stuttgart and CRC Press; 2001. Herbal drugs and phytopharmaceuticals; pp. 230–48.
- Ogie-Odia EA., Esiegebe D, Elechie MN, Erhabor J, Ogbemor E. Foliar epidermal and phytochemical studies of the grasses *Cymbopogon citratus* (Stapf.), *Axonopus compressus* (S. W. Beauv) and *Eragrostis tremula* (S. W. Beauv) in Ekpoma, Edo State, Nigeria. *Science World Journal* 2010; 6: 21–26.
- Rahman MA, Imran TB, Islam S. Antioxidative, antimicrobial and cytotoxic effects of the phenolics of *Leea indica* leaf extract. *Saudi J Biol Sci* 2013; 20:213–25.
- Rakesh S, Arunporn I. Herbal Supplements or Herbs in Heart Disease: Herbaceutical Formulation, Clinical Trials, Futuristic Developments. *J Cardiol & Cardiovasc Ther* 2017; 3(1): 555-603.
- Rao V. Modern approaches to herbal medicine. *East Pharm.* 2000; 12:35–8.
- Sagar Naskar, Upal Mazumder K, Goutam Pramanik, Malaya Gupta, Suresh Kumar RB, Asis Bala, Aminul Islam. Evaluation of the antihyperglycemic activity of *Cocos nucifera* Linn. on streptozotocin-induced type 2 diabetic rats. *Journal of Ethnopharmacology* 2011; 138:769–773.
- Semalty A, Semalty M, Rawat BS, Singh D, Rawat MS. Pharmacosomes: The lipid-based new drug delivery system. *Expert Opin Drug Deliv* 2009; 6:599–612.
- Sharma AT, Mitkare SS, Moon RS. Multicomponent herbal therapy: A review. *Int J Pharm Sci Rev Res* 2011; 6: 185–7.
- Sharvil Patil, Bhavana Choudharya, Atul Rathore, Krishtey Roy, Kakasaheb Mahadik. Enhanced oral bioavailability and anticancer activity of novel curcumin loaded mixed micelles in human lung cancer cells. *Phytomedicine* 2015; 22: 1103–11.
- Shen YJ, Zhang ZW, Luo XG, Wang XF, Wang HL. Nanoparticles of traditional Chinese herbs inhibit thrombosis in vivo. *Haematologica. Haematol Jr* 2008; 93: J1457.
- Shivananjappa MM, Joshi MK. Influence of *Emblica officinalis* aqueous extract on growth and antioxidant defense system of the human hepatoma cell line (HepG2). *Pharm Biol* 2012; 50, 497–505.
- Suba V, Murugesan T, Bhaskara-Rao R, Ghosh, L, Pal, M, Mandal SC. Antidiabetic potential of *Barleria lupulina* extract in rats. *Fitoterapia* 2004; 75: 1–4.
- Sudhanshu Kumar Bharti, Supriya Krishnan, Amit Kumar, Kaushal Kishore Rajak, Krishna Murari, Binod Kumar Bharti, Ashok Kumar Gupta. Antidiabetic activity and molecular docking of fructooligosaccharides produced by *Aureobasidium pullulans* in poloxamer-407-induced T2DM rats. *Food Chemistry* 2013; 136: 813–21.
- Sudip Sen Himani Sharma Neeta Singh. Curcumin enhances Vinorelbine mediated apoptosis in NSCLC cells by the mitochondrial pathway. *Biochemical and Biophysical Research Communications* 2005; 331: 1245-52.

Trinidad TP, Valdez DH, Loyola AS, Mallillin AC, Askali FC, Castillo JC, Masa DB. Glycaemic index of different coconut (*Cocos nucifera*)-flour products in normal and diabetic subjects. *British Journal of Nutrition* 2003; 90: 551–556.

Vetriselvan Subramaniyan, Summaiya Shaik, Anupam Bag, Gobinath Manavalan, Sarath Chandiran: Potential action of *Rumex vesicarius* (L.) against potassium dichromate and gentamicin induced nephrotoxicity in experimental rats. *Pakistan Journal of Pharmaceutical Sciences* 2018; 31(2): 509-516.

World Health Organization. WHO Guidelines for Developing Consumer Information on Proper Use of Traditional Medicines and Complementary/Alternative Medicines. Geneva, Switzerland: World Health Organization, 2004.

Wu X, Zhou QH, Xu K. 2009. Are isothiocyanates potential anti-cancer drugs. *Acta Pharmacol Sin* 2009; 30: 501–12.

Yang CS, Sang S, Lambert JD, Lee MJ. Bioavailability issues in studying the health effects of plant polyphenolic compounds. *Mol Nutr Food Res* 2008; 52(1):139-51.

Zhao HR, Wang K, Zhao Y, Pan LQ. The novel sustained-release implant of herb extract using chitosan. *Biomaterials* 2002; 23:4459–62.

Zhou Y, Chuan KB, Chen S. An information system model in Chinese herbal medicine manufacturing enterprises. *J Manufact Tech* 2005; 16: 145-155.