A REVIEW ON HERBAL DRUG NANOSUSPENSION

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ABSTRACT
Nanosuspensions are important carriers to develop a novel drug formulation. Large proportions of newly discovered drugs are water insoluble, and therefore poorly bioavailable contributing to deserted development effort. The use of drug nanosuspension is a universal formulation approach to increase the therapeutic performance of these drugs in any route of administration. Poorly water Solubility and poor bioavailability of drugs can be improved by the nanosuspension technology. Medicinal plants or their phyto-compounds are frequently considered to be less toxic and free from side-effects than synthetic drugs. But formulation aspects of Medicinal plants or their phyto-compounds are limited due to its poor water solubility. This article mainly focused on the nanosuspension plant natural products and their biological activities.

KEYWORDS: Nanosuspension, Natural products,

INTRODUCTION
More than 40% of the new chemical entities being generated through drug discovery programmes are poorly water soluble. The formulation of poorly water soluble drugs has always been a challenging problem faced by the pharmaceutical scientists.[1] There are many conventional methods such as micronization, solubilisation using co-solvents, surfactant dispersions and precipitation technique has been developed for improving solubility of poorly water soluble drugs.[2] But these techniques showed limitation to the drugs which are not soluble in both aqueous and organic solvents. Nanosuspension technology can be used to solve the problems associated with various approaches described earlier.[3]
Nano-suspension is colloidal dispersions of nanosized drug particles stabilized by surfactants. They can also be defined as a biphasic system consisting of pure drug particles dispersed in an aqueous vehicle the diameter of the suspended particle is less than 1µm in size.\textsuperscript{[4]} Reduction of drug particles to nanometer range leads to an enhanced dissolution rate due to increased surface area and saturation solubility. The nanosuspension can also be lyophilized or spray dried and the Nanoparticles of nanosuspension can also be incorporated in a solid matrix.\textsuperscript{[5]}

**Advantages of Nano-suspension Drug Delivery system**

1. It can be applied for poorly water soluble drugs
2. Physically more stable than lipososomes
3. Most cost effective
4. Reduction in tissue irritation
5. Rapid dissolution and tissue targeting can be achieved by IV route of administration
6. Improvement in biological performance due to high dissolution rate & saturation solubility of the drugs
7. Provide ease of manufacture and scale up for large scale production
8. Possibility of surface-modification of Nanosuspension for site specific delivery.
9. Improved dose proportionality\textsuperscript{[6]}

**Medicinal plants or their phyto-compounds**

Medicinal plants or their phyto-compounds may have less toxic and free from side-effects than synthetic drugs. But formulation aspects of Medicinal plants or their phyto-compounds are limited due to its poor water solubility. By considering nanosuspension formulation for medicinal plants or their phyto-compounds, it may improve the poor water solubility of medicinal plants or their phyto-compounds and can be used for investigation of biological activity.\textsuperscript{[7]}

**Nanosuspension of Natural products**

*Curcumin*

![Curcumin](image)

*Figure 1: Curcumin*
It is a natural product, which is a commonly used spice and nutritional supplement, isolated from the rhizomes of curcuma longa Linn. (Zingiberaceae). It exhibits antioxidant, anti-inflammatory, antiviral, antibacterial, antifungal, anticancer activities and has a potential against various malignant diseases, diabetes, allergies, arthritis and alzheimer’s disease etc.\cite{8} Curcumin binds with heavy metals such as cadmium and lead, thereby reducing the toxicity of these heavy metals. This property of curcumin explains its protective action to the brain. Components of turmeric are named curcuminoids, which include mainly curcumin, demethoxycurcumin and bisdemethoxycurcumin. All of these compounds are poorly soluble in water. The clinical application of curcumin is severely limited by its main drawbacks such as instability, low solubility, poor bioavailability and rapid metabolism. The nanosuspension based delivery of curcumin has been attempted to renders curcumin completely dispersible in an aqueous media.\cite{9} Curcumin nano-formulations shows superior anticancer activity compared to native curcumin. Polymer Nanoparticles based on PLGA, a biodegradable and biocompatible polymer, can produce curcumin Nanoparticles of approximately 100-200 nm size. This particle size range is small enough to allow intracapillary passage while suitable surface coating allows escape from macrophage uptake. These curcumin nanoformulations are widely studied in cell culture and animal models. Nanoparticles based on dendrimers, can produce curcumin nanoformulation which retains biological activity and has the ability to destroy human neuro-tumor cells in a selective manner.\cite{10}

**Quercetin**

\[\text{Figure 2: Quercetin}\]

It is a naturally occurring polyphenol which belongs to a group of plant pigments known as flavonoids, responsible for the colour of vegetables, fruits and flowers. Quercetin is a flavonol whose chemical structure is derived from flavone. Chemically Quercetin is known as 3,3,4,5,7-pentahydroxyflavone. Particularly rich sources for quercetin are onions, apples and tea.\cite{11} It possess a wide array of biological effects that are considered beneficial to
health, including anti-oxidative, free radical scavenging, anti-carcinogenic, anti-inflammatory and antiviral activities. But the clinical application of quercetin is limited due to its poor solubility and dissolution rate. Thus the quercetin nanosuspension has been developed to improve the solubility and dissolution rate of drug.\textsuperscript{[12]} The 2,2-diphenyl -1-picrylhydrazyl hydrate(DPPH) radical scavenging assay is routinely practiced for the assessment of the antioxidant activity of the compounds. The method is based on the discoloration due to the reaction that occurs between radical and antioxidant, which can be determined spectrophotometrically. In the study quercetin showed significant antioxidant activity compared with that of standard ascorbic acid. The 3-(4,5-dimethylthiazol-2,5-diphenyltetrazolium bromide) dye reduction assay was conducted to diagnose the cytotoxicity activity of Quercetin and formulated Quercetin nanosuspension at different concentrations. The result shows quercetin nanosuspension exhibited significant antitumor activity against Dalton lymphoma cells at dose dependent manner.\textsuperscript{[13]}

\textit{Coriander sativum}

\begin{figure}[h]
\centering
\includegraphics[width=0.5\textwidth]{coriander.jpg}
\caption{Coriandrum sativum L.}
\end{figure}

Coriander (\textit{Coriandrum sativum} L.) being an annual herb, extract was isolated from the whole plant of \textit{coriander sativum}. Its plant seeds, leaves and roots are edible, although they have distinct flavours and uses. Coriander can be used as whole plant and can be processed because of its perishable nature of leaves and to increase the palatability of ripe fruits before using it as flavouring agent in different food preparations.\textsuperscript{[14]} Coriander plant is a rich reservoir of micronutrients and nutritional elements. Coriander is also well known for its anti-oxidant, anti-diabetic, anti-mutagenic, anti-anxiety and antimicrobial activity along with analgesic and hormone balancing effect that promotes its use in foods due to numerous health benefits and its protective effect to preserve the food for longer period.\textsuperscript{[15]} Hepatotoxicity is the major factor responsible for drug withdrawal from the market. In the study investigated
the nanosuspension containing coriander sativum extracts against the hepatotoxic activity. Results shown that the nanosuspension shows very significant effect on hepatotoxic liver of male Wistar albino mice induced by Carbon tetra chloride.[16]

**Phyllanthus amarus**

*Phyllanthus amarus* is a plant of the family Euphorbiaceae and has about 800 species which are found in tropical and subtropical countries of the world. It is commonly used for traditional Indian medicine and as dietary adjuncts for the treatment of numerous physiological disorders including hepatic disorders. *Phyllanthus amarus* is a branching annual glabrous herb and is widely distributed as a weed in cultivated and waste lands. Due to the poor water solubility of its major constituents such as lignans and flavanoids, its absorption upon oral administration could be limited. Hence the nanosuspension of *phyllanthus amarus* developed for improving solubility of the drug. Investigation of hepatoprotective effects of the ethanolic extract of *Phyllanthus amarus* extract (PAE) and its Nanoparticles (PAN) on paracetamol induced acute liver toxicity carried out in Sprague-Dawley rats. It was found that an oral dose of PANs that is five times less than the oral dose of PAE showed a similar hepatoprotective effect by reducing levels of aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase and bile salts. These biochemical assessments were supported by rat hepatic biopsy examinations.[17]

**Berberine**

![Figure 4: Berberine](image)
Berberine, an isoquinoline derivative alkaloid and active ingredient of coptis, exhibit a wide spectrum of pharmacological activities. It has been used in traditional Chinese medicine and Ayurvedic medicine. Berberine along with its derivatives or in combination with other pharmaceutically active compounds or in the formulations has applications in various therapeutic areas such as cancer, inflammation, diabetes, depression, hypertension and various infectious areas. But the clinical application of berberine is limited due to its poor oral bioavailability.[18] Antidiabetic effects of Berberine nanosuspension relative to efficacy of bulk Berberine were evaluated in diabetic mice models. Moreover, Berberine nanosuspension produced superior hypoglycaemic and total cholesterol and body weight reduction effects compared to equivalent dose of bulk berberine and metformin. Therefore the delivery of berberine as a nanosuspension is a promising approach for treating type 2 diabetes.[19] Hepatocarcinoma, a malignant cancer, threaten human life badly. Both in vitro and in vivo anti-hepatocarcinoma effects of berberine nanosuspension relative to efficacy of bulk Berberine were evaluated. Berberine nanosuspension exhibited significant inhibitory effects against human HepG2 and Huh7 cells where as in vivo studies also showed higher antitumor efficacy. Therefore the delivery of berberine as a nanosuspension is a promising approach for treating hepatocarcinoma.[20]

_Cuscuta chinensis_

_Cuscuta chinensis_ is a commonly used traditional Chinese medicine to nourish the liver and kidney. It is a parasitic plant belongs to convoluceae. It is commonly used as an anti-aging agent, anti-inflammatory agent, pain reliever and aphrodisiac. Due to the poor water solubility of its major constituents such as flavonoids and lignans, its absorption upon oral administration could be limited. Hence the nanosuspension method was used to improve the solubility of the drug.[21] The hepatoprotective and anti-oxidant effects of ethanolic extract (CE) of _Cuscuta chinensis_ was investigated on acetaminophen-induced hepatotoxicity in rats.
It was found that an oral dose of *Cucuta chinensis* nanosuspension that is 5 times less than the oral dose of *cuscuta chinensis* extract showed similar hepatoprotective activity. In addition, the anti-oxidant activities of CE and CN both significantly increased superoxide dismutase, catalase, glutathione peroxidise and reduced malondialdehyde. Moreover results showed that the hepatoprotective and anti-oxidant effects of *Cuscuta chinensis* nanosuspension was effectively better than *Cuscuta chinensis* extract.[22]

**Camptothecin**

![Camptothecin](image)

*Figure 6: Camptothecin*

Camptothecin is a cytotoxic quinoline alkaloid which inhibits the DNA enzyme topoisomerase. It was isolated from the bark and stem of Camptothecia acuminate, a tree native to china used as a cancer treatment in traditional Chinese medicine. Camptothecin showed remarkable anticancer activity in preliminary clinical trials but also low solubility and high adverse drug reaction.[23] *In vitro* and *in vivo* antitumor efficacy and the dose dependent toxicity of camptothecin nanosuspension comparing with that of topotecan were studied. The cytotoxicity of camptothecin nanosuspension and topoecan was investigated against MCF-7, HCT-8 and PC-3 cells using MTT assay, antitumor activity in vivo were evaluated against HCT-8 xenograft model, and the dose dependent toxicity in vivo during the treatment were investigated by body weight changes and relative organ weight variations. Camptothecin nanosuspension presents about 6 times in vitro cytotoxicity active than TPT against cell lines MCF-7, nearly the same in vivo antitumor activity and lower toxicity. The results confirm that camptothecin nanosuspension is a novel potential formulation with high antitumor efficacy and low toxicity.[24]

**CONCLUSION**

The poorly water soluble drugs have always been a challenging problem faced by pharmaceutical scientists. In this case nanosuspension formulations can be considered as promising candidate. Medicinal plants are mainly used for traditional Indian medicine and as
dietary adjuncts for the treatment of numerous physiological disorders including hepatic disorders. Due to the poor water solubility of its major constituents, its absorption could be limited. Therefore, nanosuspension technology is able enough to bring enormous immediate benefits and will revolutionize the Ayurvedic research. By emphasizing this technology, our society will be benefited financially also.

REFERENCES


