

# Impact of nanotechnology on global trade of herbal drugs: An overview

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## Abstract

Natural herbs are moving from fringe to mainstream use with a increase number of population-seeking remedies and health approaches free from hazardous side effects caused by laboratory synthesize chemicals. Recently, focus has been given to utilize eco-friendly and bio-friendly natural-based products for the prevention and cure of diseases. It is documented that 80% of the world's population has belief in natural medicine, particularly plant-based drugs for their primary healthcare. Herbal drug generally introduce in the market in traditional dosage form but now different scientific approaches are being developed these days to deliver herbal medicines due to their poor rate of absorption and target specific approach. Novel drug delivery systems including nanoparticles have been developed for the effective delivery of herbal drugs. Nanoparticulate formulations such as liposomes, polymeric nanoparticles, micro-emulsions, proliposomes, and solid lipid nanoparticles present potential to deliver herbal medicines effectively. Because of nanotechnology, the use of herbal drug is greatly increased in recent years. In this article, we are try to elaborating the role of nanotechnology which increases the potential as well as sale of herbal drugs in global world.

**Key words:** Commercial, herbal, nano particle, nanotechnology, trades

## INTRODUCTION

Nowadays, there has been a change in global trend from synthetic to natural medicine, which we can say "back to nature." The efficiency of medicinal plant species, or herbal medicine, depends on the active molecules present since they provide synergistic action and thus enhance the therapeutic effectiveness.<sup>[1]</sup> Most of the herbal actives are poorly absorbable because of their hydrophobic behavior. This nature of constituents leads to decreased bioavailability and increased systemic clearance thus required repeated administration or increased dose, and thus limits the clinical use of herbal medicines.<sup>[2]</sup> Therefore, new carriers should deliver the active chemical molecule at a enough concentration during the entire period of treatment and direct it toward the specific target, because these requirements are not completely obtained by conventional treatments.<sup>[3]</sup> Decrease or complete loss of activity can be observed when constituents of an extract are isolated or purified. Moreover, some components are highly sensitive to the acidic pH of the stomach, which promotes their destruction, and loss of the desired effect, after

ingestion. Some extracts are not used clinically because of these obstacles.<sup>[4]</sup>

Many novel drug delivery strategies, such as microemulsion, solid lipid nanoparticles (SLNs), polymeric nanoparticles, liquid crystal (LC) systems, liposomes, precursors systems for LC, and have attempted to break this barrier; they allow substances with different properties to be used in the same dosage form, and may even change a substance's physical properties and behavior in a biological environment.<sup>[5,6]</sup> This technological discovery has been a revolutionized drug delivery. The novel drug delivery systems (NDDS) have the ability not only to increase the potency of active components but also to reintroduce other constituents that were discarded because they were not beneficial in formulation.<sup>[7,8]</sup> Moreover, the ability to improve new substances, such as by increasing specificity

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and efficacy, protecting against thermal- or photo-degradation, minimize the side effects, and controlling the rate of release of constituents, before they are launch to the market or used therapeutically, makes this approach even more valuable.<sup>[9-12]</sup>

There are many of the herbal products and their derived constituents present in the market are: Lovastatin (anticholesterolemic),<sup>[13]</sup> paclitaxol, doxorubicin (both anticancer drugs), cyclosporine-A and tacrolimus (both immunosuppressive),<sup>[14,15]</sup> erythromycin, streptomycin, rifamycin (all antibiotics), and amphotericin-B (fungicidal). Actually, with respect to the conventional pharmaceuticals, these drugs have their existence from natural remedies. Many drugs (e.g., digoxin, quinine, morphine, atropine, aspirin, bromelain, salbutamol, colchicine, etc.) had been extracted from the plants as their active molecule for treating various diseases.<sup>[16-18]</sup> From the opium popy (*Papaver somniferum*) morphine was isolated as a first drug by serturner. Quinine extracted from the cinchona tree (*Cinchona officinalis*) is used to treat malaria, and from willow bark aspirin was isolated is used for the treatment of fever.<sup>[19]</sup> Most of the plants and formulations (e.g., colchicine, curcumin, triphala, pomegranate, guggalosterone, sariva, etc.) have explored the potential to cure cancer and inflammation.<sup>[20]</sup>

## COMMERCIALIZATION OF HERBAL

Commercialization efforts in herbal medicine by nanotechnology have now started around the world. Of the 300 companies identified being actively involved in nano formulation worldwide, 259 are start-ups and Small and medium-sized enterprises (SME) that focus on the development of nanotechnology-enhanced phyto pharmaceuticals and medical equipments and devices. Further, 41 another major pharmaceutical and medical device corporations have nanomedicine products on the market or run development projects in which nanotechnology plays a vital role.<sup>[21,22]</sup> Over the past decade, 38 nanotechnology-enhanced medical products were placed on the market with estimated total sales of EUR 5.4 billion in 2004.<sup>[23,24]</sup>

## WORLDWIDE TRADE OF HERBAL OR NATURAL OCCURRING DRUGS

The world market for phyto medicines currently stands at over \$60 billion annually. The sale of natural-based medicines is expected to get higher at 6.4% on an average annual growth rate.<sup>[25]</sup> Due to the effect of many factors, the market of herbal medicines has grown at an expressive rate globally. Some of them are: Preference of consumers for natural therapies; concern regarding undesirable side effects of synthetic medicines and the faith that herbal drugs are free from unwanted effects, since most of the people worldwide have been using natural medicines for thousands of years; great interest in alternative medicines; preference of populations for preventive medicine due to increasing population age;

the belief that natural medicines might be of effective benefit in the treatment of various critical diseases where conventional therapies and medicines have proven to be inadequate; tendency toward self-medication; improvement in quality, proof of efficacy, and safety of herbal medicines and high cost of synthetic medicines.<sup>[3,4]</sup> According to the World Health Organization, herbal medicines are lucrative globally and they represent a market value of about US\$43 billion a year.<sup>[26]</sup> According to an estimate in 1991, the herbal medicine market in the European countries was about \$6 billion, with Germany accounting for \$3 billion, France \$1.6 billion, and Italy \$0.6 billion while in other countries was 0.8 billion. In 1996, the herbal medicine market in the European countries was about \$10 billion, in the USA about \$4 million, in India about \$1.0 billion and in other countries was \$5.0 billion.<sup>[27]</sup> This market is followed by France, \$1.8 billion; Italy, \$700 million; the United Kingdom, \$400 million; Spain, \$300 million; the Netherlands, about \$100 million, In 1997, the European market alone reached about \$7.0 billion. The German market corresponds to about 45% of the European market, about \$2.8 billion [Table 1 and Figure 1].<sup>[28,29]</sup>

## NEED FOR NDDS “NANO CARRIERS” FOR “HERBAL REMEDIES”

The activity of herbal drugs is depends on overall function of active components, as all the constituents provide synergistic

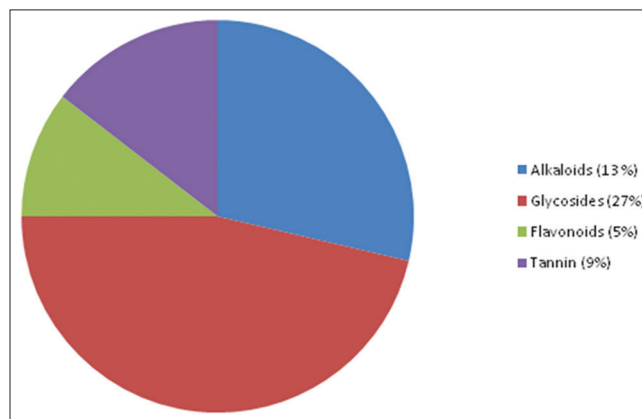


Figure 1: World trade of important plant-based medicinal constituents in year 2012

Table 1: Global herbal market

Market	Size (US\$ billion)	Percentage
European union	28	45
Rest EU	2.4	4
ASEAN	10.8	19
Japan	9.8	16
North America	6.9	11
Others	4.1	7
Total	60	100

action and thus enhance the therapeutic efficiency. Each every active moiety plays an vital role and they are all related to each other.<sup>[30]</sup> However, most of the herbal origin drugs possess low lipid solubility character leading to lower bioavailability and increased systemic clearance requiring frequent administration or higher dose, which makes the drug as a poor candidate for therapeutic use. The discovery of nanotechnology is consider as a milestone in medicine world.<sup>[31,32]</sup>

In case of herbals, nanotechnology becomes a great remedy to overcome the problems arising nowadays. In herbal formulation research, developing nanodosage forms has large number of advantages for herbal drugs, including increase in the solubility and bioavailability, prevention from toxicity, greater biological activity, enhancement of stability, improving tissue macrophages distribution, controlled delivery, protection from physical and chemical degradation, and changes [Table 2].<sup>[33,34]</sup>

Herbal remedies were selected as drug candidates for delivery through a nano delivery system because many effective molecules soluble in chloroform, petroleum ether, acetone, and methanol are not will be suitable for delivery as such.<sup>[35]</sup>

In addition, these are the bulk drugs so dose reduction is intended. Currently, marketed herbal conventional formulations lack target specificity for various chronic diseases and having certain side effects so nano technology will be the useful tool to overcome the above problems.<sup>[36,37]</sup>

### Strategies of Nanotechnology as NDDS

Drug delivery system fetched NDDS, a novel approach to overcome the drawbacks of the traditional drug delivery

systems.<sup>[38]</sup> Nano-sized delivery system was selected because they appear to be able to deliver high concentrations of drugs to disease sites because of their unique size and high loading capacities<sup>[39]</sup> also, the deliver the drug in the small particle size that enhances the entire surface area of the drugs allocating quicker dissolution in the blood.

The NDDS shows enhanced permeation and retention effect, i.e., enhanced permeation through the barriers because of the small size and retention due to poor lymphatic drainage such in tumor.<sup>[40]</sup> In addition, another aspect of selection of NDDS, as they exhibits passive targeting to the disease site of action without the addition of any particular ligand moiety.<sup>[15]</sup> In addition, they reduce the frequency, dose, and the side effects.<sup>[41]</sup>

## RECENT DEVELOPMENT

The nanoparticles now has been comes as the capable approach in drug delivery systems for the well-organized delivery of herbal drugs utilized in the treatment of many critical diseases such as cancer by crossing the reticulo-endothelial system, increased permeability and retention effect, and tumor-specific targeting.<sup>[42]</sup>

Recently, pharmaceutical researcher has shifted their focus to designing a drug delivery system for herbal medicines using a modern approach. *Cuscuta chinensis* is a commonly used traditional Chinese medicine to nourish the liver and kidney. The oral absorption of drug is limited its chemical constituents such as flavonoids and lignin.<sup>[43,44]</sup> Hence, the nanoparticles for the same were developed,<sup>[45,46]</sup> work has also

**Table 2: Commercial nanoparticles for bio applications<sup>[14,16,26,37]</sup>**

Drug delivery	Polymeric nanoparticles engineered to carry antitumor drug
Pharmaceutical coating to improve solubility of drug	Layer-by-layer poly-electrolyte coating, 8-50 nm
Drug delivery	Reduce drug particles size to 50-100 nm
Luminescent biomarkers	Semiconductor quantum dots with amine or carboxyl groups on the surface, emission from 350 to 2500 nm
Tracking and separation of different types of cells	Magnetic core surrounded by a polymeric layer coated with antibodies for capturing cell
Drug delivery	Antimicrobial nanoemulsion
Drug delivery	Micellar nanoparticles for encapsulation of drugs, proteins, and DNA
Drug delivery	Polybutylcyanoacrylate nanoparticles are coated with drug and then with surfactant can go across the blood brain barrier
Gold nanoparticles for biological markers	Gold nanoparticles bio-conjugates for TEM and/or fluorescent microscop
Gold biomarkers	DNA barcode attached to each nanoprobe for identification purposes, PCR used to amplify the signals, also catalytic silver deposition to amplify the signal using surface plasmon resonance
Drug delivery	Nanoparticles for drug delivery

PCR: Polymerase chain reaction, TEM: Transmission electron microscopy

**Table 3:** List of phytoconstituents modified by nanotechnology<sup>[11,12,19,31]</sup>

Approach	Experimental work was done	Significance
Curcuminoids	Enhance curcuminoids bioavailability and reduce perceived toxicity	Improved cellular uptake, enhanced dissolution rates, excellent blood stability, controlled release functions, multifunctional design, enhancement in its pharmacological activities (e.g., antioxidant and antihepatoma activities) etc.
Berberine hydrochloride	Anticancer activity and novel mechanisms have been explored, the chance of regulating glucose and lipid metabolism in cancer cells showing more potential than ever	In recent years, the pharmaceutical preparation of berberine hydrochloride has improved to achieve good prospects for clinical application, especially for novel nanoparticulate delivery systems
Colchicine	The effect of eugenol on intestinal absorption of colchicine in an oral administrative nanoemulsion formulation	Relative bioavailability of nanoemulsion and eugenol–nanoemulsion were enhanced by about 1.6- and 2.1-fold
Genistein	Newer formulations of genistein such as diindolylmethane (BDIM) from Bioresponce Inc. has shown some enhanced bioavailability	Genistein has been shown to possess anticancer activities
Resveratrol	Resveratrol (3, 5,4'-trihydroxy-trans-stilbene) is a phytoalexin produced naturally by several plants when under attack by pathogens such as bacteria or fungi	The earliest reported nano formulation of resveratrol comes from a study by Yao <i>et al.</i> , where they prepared resveratrol chitosan nanoparticles with free amine groups on the surface so as to conjugate ligands, which will actively target to special tissues or organs

been carried out in the development and characterization of SLNs for the traditional Chinese medicine for their targeted delivery and increased bioavailability and efficacy.<sup>[47,48]</sup> A recent experimental study of polylactic acid nanoparticles of lipophilic anti-cancer herb drug (cucurbitacins and curcuminoids) using a precipitation method have been developed [Table 3].<sup>[14,49]</sup> In the recent years, nanostructured carrier systems such as micro-emulsion, polymeric nanoparticles, liposomes, sliver nano materials, SLNs, polymeric micelles, nano-emulsions, micro sphere have been discovered for their potential to deliver anticancer drugs by oral route.<sup>[17,50,51]</sup> Moreover, the oral route offers great potential for delivery of cytotoxic agents and therefore the attention has focused on the development of oral dosage forms for chemotherapy in oncology.<sup>[18,52,53]</sup>

## FUTURE PROSPECTS OF NANOMEDICINES

Herbal remedies and nutraceutical products research is more familiar worldwide. The development of phyto medicine in the drug delivery system in a number of organizations is being carried out at basic and clinical trial levels.<sup>[54,55]</sup> To improve the proper delivery systems at the sites or locations in the whole body in a particular dose will not compromise with the existing treatment.<sup>[56]</sup> This would not only give relieve from unwanted effects such as toxicity and hypersensitive reactions but also will increase the patient's strength internally is very much confidence boosting which is desirable. In the future, the concept of herbal nanoparticles for the treatment of critical

diseases such as cancer, diabetes mellitus, and anemia drug delivery may also fascinate some potential research groups and potentially create attention grabbing results.<sup>[57,58]</sup>

## CONCLUSION

Hence, using “herbal therapy” in the form of nanocarriers will definitely increase its potential for the treatment of many chronic diseases and health benefits. Many successful examples were observed with the direction of nano research. Natural remedies are also prosperous resources of advantageous compounds holding antioxidants and constituents that can be made use in purposeful foods. This type of research among the traditional “herbal remedies” and newer approaches of modern drug delivery system, i.e., “nanotechnology” has the lucrative or attractive therapies to the pharmaceutical in the near future that will enhance health of people. It is anticipated that the effective and valuable relevance of the natural products and herbal remedies being applied with the nano carrier will enhance the significance of existing drug delivery systems.

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