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Nanophytomedicines: A Novel Approach to Improve Drug Delivery and Pharmacokinetics of Herbal Medicine

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ABSTRACT: Novel drugs delivery systems, formulations from plant actives and extracts are still a matter of thrust and hot cake among the current researchers. Nanophytomedicines are prepared from active phytoconsituents or standardized extracts. In this area, novel delivery systems such as polymeric liposomes, colloidisomes, aquasomes, ethosomes, niosomes, proliposomes, phytosomes, nanoparticles, nanocapsules, nanoemulsions, microsphere and transferosomes have been proven to be a better carrier for delivery of the phyto-constituents by recent researches. Due to improved bioavailability, protection from toxicity, enhanced pharmacological activity, better stability, improved tissue macrophages distribution, sustained delivery, and protection from physico-chemical degradation, novel delivery systems are more suitable delivery system in compare to the conventional systems. Present paper attempts to spotlight recent trends or approaches in development of nanophytomedicines.

Keywords: Nanophytomedicines, Bioavailability, Bioactivity, Nanotechnology, Drug delivery

INTRODUCTION

Plenty of the drugs in current usage are derived either directly from natural sources or are chemical analogues of natural origin molecules. The primary handicap in harnessing the hitherto unrealized potential of phytomedicines has often been the poor in vivo response of actives that have otherwise demonstrated excellent in vitro pharmacological activity. The reasons have been manifold; ranging from poor solubility profiles and impaired membrane permeability to inadequate deposition of drug at the site of action. Novel drug delivery systems are increasingly being applied as effective tools in overcoming these issues and helping design physiologically effective phytoformulations (Mukne *et al.,* 2017; Saraf *et al.,* 2015). The ideal drug delivery system should be able to target the drug release at the site of action in a controlled manner so as to obtain optimum therapeutic effect with minimal side effects. Various nano-particulate and vesicular platforms, including polymeric, lipoidal and macromolecular types, have been deployed for achieving these end-points. Nanophytomedicines are prepared from active phytoconsituents or standardized extracts. Their developments, advancements and avenues are being discussed in present article.

METHODOLOGY

The approach consisted to search several resources, including Books, Theses, Technical Reports, Conference proceedings, web-based scientific databases such as publications on PubMed, Science direct, Springer, ACS, Scielo, PROTA, Google, Google scholar, MEDSCAPE, BMC, MEDLINE, Pubmed, SCOPEMED, and other allied databases covering fields of pharmacology and biomedicine. The search criterion was aimed to probe recent approaches in

drug development apropos nanophytomedicines, in light of published reports. Searches were not limited by date or place of publications but to publications available in English. Present report examined the available literature up to March 2017.

RESULTS

Phytomedicines are gaining popularity these days owing to their natural origin and less side effects. Herbal powders, extracts or isolated active phytoconstituents, despite of impressive *in-vitro* activity, generally show least or non-significant efficacy in *in-vivo* investigations due to their poor solubility (aqueous/lipid) and stability, poor lipid solubility, non-uniform particle size, poor absorption and bioavailability, destruction of few plant extracts in gastric juice (during gastric emptying), rapid clearance and biotransformation. A number of nanotechnology approaches and novel drug delivery systems, such as liposomes, niosomes, nanospheres and phytosomes have been investigated to improve the herbal drug delivery (Abhinav *et al.,* 2016). Applications of nanotechnology have been reported potentially effective in improving the bioavailability and bioactivity of phytomedicines. Some of the key advanced methods that can be adopted are: (I) Reducing particle size of phytomedicines to nanosize (Li *et al.,* 2012), (II), Attaching certain polymers of micro/nano materials with phytomedicine (Li *et al.,* 2009; Yadav *et al.,* 2011) (III) Using nano-structured carrier systems for phytomedicines (Zhao *et al.,* 2010) and (IV) Modification of surface properties of phytomedicines (Chen *et al.,* 2009; Tiwari *et al.,* 2012). Surface properties of phytomedicines can be modified by coating with hydrophilic, stabilizing, mucoadhesive polymers or surfactants.

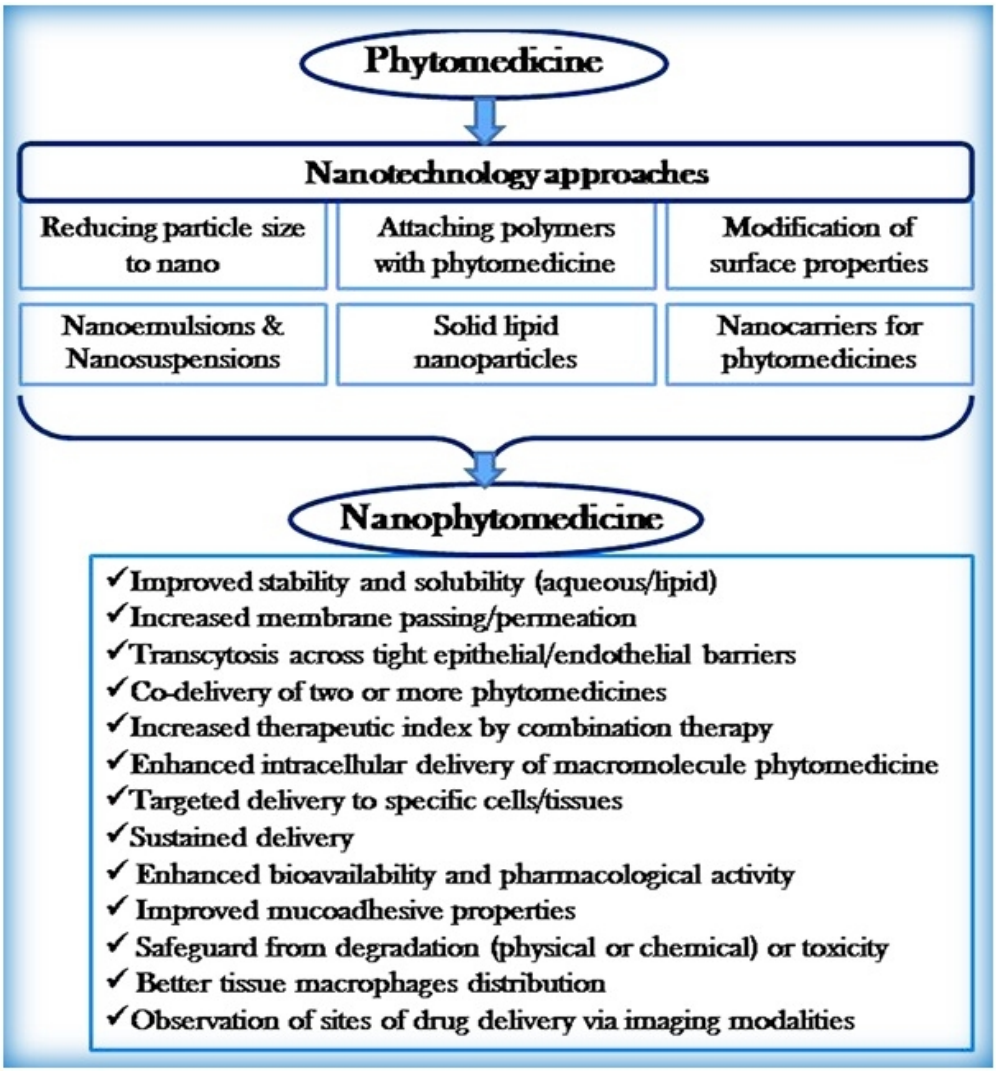

Fig. 1. Application of nanotechnology on phytomedicine and its benefits.

These methods modify the zeta potential of nanoparticles, improves stability and particle uptake (Tiwari *et al.,* 2012). Evidences suggest that incorporating nanotechnology in formulation of phytomedicine may be likely to provide several advantages (Fig.1) (Sahni *et al.,* 2011; Jain *et al.,* 2011; Lambert, 2010, Liong *et al*., 2008). Several reports elucidated improved biological activity and therapeutic potential of phytomedicines by integrating nanotechnology approaches and converting them to nanophytomedicines. For instance, nanosized herbs such as *Cuscuta chinensis* (prepared by nano-suspension method) and *Radix salvia* (prepared by spray drying method) shown improved bioavailability, biological actions, and manifold reduction in therapeutic dose (Yen *et al.,* 2008; Su *et al.,* 2008). Nano emulsified ethanolic extract of *Phyllanthus amarus* Schum & Thonn showed better hepatoprotective activity than *Phyllanthus amarus* Schum (100 mg/kg body weight) and also repeated dose oral toxicity proved to be safe (Deepa *et al.,* 2012).

Table 1: Examples of recent developments in nanophytomedicines.

Medicinal plant	Nano-formulations	Method	Active ingredient	Rationale	Therapeutic targets studied	Ref.
Trypterygium wilfordii Hook F	Celastrol nanoparticles	Poly (ethylene glycol)-block-poly (ε -caprolactone) nanopolymeric micelles	Celastrol	To improve the hydrophilicity	Retinoblastoma therapy	Su *et al.,* 2008
Boswellia caraterii and *Commiphora myrrha*	Solid lipid nanoparticles	High-pressure homogenization method	Frankincense and myrrh essential oils	To improve the hydrophilicity & bioavailability	Antitumor efficacy	Deepa et al., 2012
Curcuma longa	Glyceryl monooleate nanoparticles	High-pressure homogenization method	Curcumin	To enhance bioavailability in brain tissue	Glioblastoma therapy	Li *et al.,* 2012
Ginkgo biloba	PEGylated nanoparticles	Co-encapsulation	Ginkgolides A, B, C and bilobalide	Sustained and synchronized release of the four components	-	Shi *et al.,* 2012
Scutellaria baicalensis Georgi	Pulmonary nanocrystal	Anti-solvent recrystallization followed by high pressure Homogenization	Baicalein	To enhance the bioavailability	-	Kundu *et al.,* 2012
Salvia miltiorrhiza Bunge	Tanshinone IIA nanoemulsions	Emulsification/high pressure homogenization	Tanshinone IIA	To improve the hydrophilicity & bioavailability	Cytotoxicity evaluation against human bladder cancer cells	Han *et al.,* 2012
Salvia miltiorrhiza Bunge	Solid lipid nanoparticles	Ultrasonic and high-pressure homogenization method	Cryptotanshinone	To improve the bioavailability	-	Zhang *et al.,* 2011
Kaempferia parviflora	Solid lipid nanoparticles	Oil-in-water microemulsion	Extract of Kaempferia parviflora	To enhance their transdermal permeability	-	Chang *et al.,* 2011
Strychnos nux-vomica	Polylacticacid nanoparticles	Solvent diffusion method	Brucine	Sustained release	-	Hu *et al.,* 2010
Artemisia annua L.	Artemisinin nanocapsules	Self assembly procedure	Artemisinin	To increase the biovailability	Anticancer therapy	Yadav *et al.,* 2011
Panax notoginseng	Panax notoginsenoside-loaded core-shell hybrid liposomal vesicles	Water-in-oil-in-water double emulsion solvent evaporation method	Panax notoginsenoside	To increase the bioavailability and to enhance its protective effects	Protective effects on cerebral ischemia/reperfusion injury and acute myocardial ischemia	Sutthanut *et al.,* 2009

Likewise, few more developments in nanophytomedicines have been observed recently (Table 1) (Li *et al*., 2012; Shi *et al.,* 2012; Kundu *et al.,* 2012; Han *et al.,* 2012; Zhang *et al.,* 2011; Chang *et al.,* 2011; Hu *et al.,* 2010; Sutthanut *et al.,* 2009; Zhao *et al.,* 2009; Zhang *et al.,* 2012).

CONCLUSION

Present report reflects promising future of nanophytomedicines to enhance the bioactivity and surmount the concerns associated with herbal medicines. Nevertheless, limited works on nanophytomedicines are available, and majority of such investigations are carried out on phytomedicine of Chinese or Thai origin. The benefits of nanophytomedicines are indubitable and unstoppable; and there is a pressing need to encourage such researches in Indian setting to explore vast potential of Ayurvedic medicinal plants.

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