NANOPHYTOMEDICINE AND DRUG FORMULATIONS

RAJATH OTHAYOTH, SRAVYA KALIVARAPU & MAHENDRAN BOTLAGUNTA
Department of Biotechnology, Centre for Biomedical Research, K.L. University,
Guntur, Andhra Pradesh, India

ABSTRACT

Nanophytomedicine is a new emerging area in the field of Ayurvedic Medicine, which allows encapsulating the active phytoconstituents of medicinal plants to treat not only communicable diseases but also non-communicable diseases like cancer and diabetes. Cancer is a deadly disease and the recurrence of cancer is unexpected, because the current therapeutic approaches are unable to effectively deliver the drugs into the tumor environment. The non-specific release of the drug potentially can lead to non-specific cell interactions and they further eventually may damage body’s immune surveillance program. Therefore, it is utmost important to identify and encapsulate potential phytochemical constituents induce tumor cell death with minimal side effects. Nano-encapsulated phytoconstituents has shown to increase the bioavailability of water soluble and insoluble therapeutic compounds by adapting various combinatorial drug formulations. The present review discusses about the various kinds of drug formulations for the delivery of active phytoconstituents to treat deadly diseases to human kind.

KEYWORDS: Drug Formulation, Nanophytomedicine, Phytoconstituents, Therapeutic Compounds

INTRODUCTION

Nanotechnology is a modern technology and is being used in almost all industry for the development of cost effective and eco-friendly products. Different nanomaterials containing products are started to available in the world markets like coatings, computers, clothing, cosmetics, sports equipment, food processing devices and medical devices. It is mainly due to the technology is in conjunction with multi-disciplinary areas of science such as medicine, electronics and robotics. On the other hand, this technology is used to manufacture tools for the aerospace research and Mars exploration. Typically the ‘nano’ means small size and it ranging from 1-100 nm. The smallest size is glucose molecule (1 nm) and the biggest size is Herpes virus (100nm), because of their small size they can accommodate and they can be easily altered at any laboratory conditions (Dowing, et al., 2004). In this article, we address the importance of nanotechnology in the field of phytomedicine, there after coined as nanophytomedicine.

Ayurveda or phytomedicineis one of the oldest forms of health care known to mankind which uses various phyto compounds such as alkaloids, steroids, tannins and flavonoids from medicinal plants to treat various human ailments. The flavonoids, alkaloids and glycosides has shown to be responsible for cure diabetes, obesity, inflammation associated diseases, cardiovascular diseases and cancer (Yadav et al., 2011). Incorporation of the Ayurvedic drugs into novel formulation systems is developed to overcome the toxicity issues to treat human ailments in respect to both communicable and non-communicable diseases (Figure 1).

The activity of Ayurvedic drugs loaded nanoparticles are depend up on the overall function of a variety of components present in the certain systems (Table 1). Each compounds shows different properties when it was added
synergistically. However, most of the drugs possess lower bioavailability and increased systemic clearance. In Nanophytomedicine research, developing of different dosage formulations with the help of different nanomaterials such as Nanocapsules, Nanogels, Herbal nanoparticles, Nanoparticles, Nanopaste, Nanopowder and Nanoemulsions has large number of advantages for Ayurvedic drugs like high solubility, better bioavailability, lesser toxicity, good pharmacological activity and high stability (Figure 2). These formulations are used for improving sustained delivery and protection from faster chemical degradation. So the Nanophytomedicines have a potential future in the field of modern medicine (Suri et al., 2007).

**AYURVEDIC DRUG FORMULATIONS**

**Nano-Capsules**

Ayurvedic nanocapsules are the herbal drug containing nano shells made with a nontoxic polymer. These nanocapsules are used for controlled drug delivery at a specific site in a targeted manner. The type of polymers used for herbal nanocapsules preparations are Poly-e-caprolactone (PCL), poly (lactide) (PLA), and poly (lactide-co-glicolide) (PLGA). The application of nanocapsules in herbal medicine is because of their small size and high surface area to volume ratio, and also it improves pharmacokinetic and bio distribution for therapeutic agent by nano particles drug carriers. They can bypass blood barrier and also improves the solubility of hydrophobic compounds as well as they increase the stability.

The plant compounds with drug characters can be easily encapsulated in to these polymers based emulsification technique. The compounds such as gallic acid, protocatechuic acid and isoflavone are loaded inside the biodegradable nanocapsules (Yilmaz et al., 2004). These nanocapsules showed good anti-inflammatory and blood compatibility properties. The loading of different types of Ayurvedic Bhasma’s like Muktashukthibhasma and swarnabhasma are studied with the help of nanocapsules (Kumar et al., 2006).

**Ayurvedic Nanoparticles for Cancer Therapy**

The applications of ayurvedic nano drugs in cancer therapy results in targeted drug delivery with enhanced therapeutic efficiency and also with low side effects .This concept was widely accepted and it has some limitations due to lack of availability of technology and it may causes risk for the process of validation . Ayurvedic cancer nanotechnology (1-100nm size range) can change the foundations of the cancer treatment, diagnosis and detection. Nowadays one of the major leading causes of the cancer, the repeated chemotherapeutic treatment resulted in tumours that are resistant to these agents. So it is very useful to identify the natural products that targets and multiply signaling pathways as well as growth inhibitory effects on human cancer cells without have a result in toxicity issues in the normal cells.

In Ayurvedic nano materials, especially the gold bhasmas nanoparticles have unique physicochemical properties such as biocompatibility and ease of surface functionalisation. The most chronic illness, including cancer, diabetes and cardiovascular and pulmonary diseases are mediated through chronic inflammation. And it has the potential to delay the suppressing chronic inflammation, prevent and treat various chronic diseases, including cancer (Huang et al., 2009). Various nutraceuticals from fruits, vegetables, vitamins, spices and Chinese and ayurvedic medicine shown to safely suppress proinflammatory pathways; their low availability invivo limits shows their use in preventing and treating of cancer (Zhong et al., 2009).
The Nanocurcumin, polymeric nanoparticle formulation of curcumin is used to treat the medulloblastoma and glioblastoma cells (Bisht et al., 2007). This curcumin has minimal systemic bioavailability, but its biologic activity and bioavailability have been tremendously increased via various nanoparticle formulations. The studies proved that Nanocurcumin has good anti-inflammatory and anticancer properties (Kumar et al., 2003). Beside the Nanocurcumin, the potential of red chili (capsaicin), cloves (eugenol), ginger (zerumbone), fennel (anethole), kokum (gambogic acid), fenugreek (diosgenin), and black cumin (thymoquinone) in cancer prevention has been studied. The phyto drugs like Taxol, Artemisinin, Berberine and Camptothecin are loaded in the polymeric nanoparticles for the treatment of various tumors (Aggarwal et al., 2008). The Ursolic acid (UA), another poorly soluble natural product, is a triterpenoid with a wide variety of antitumor activities. The Ursolic acid loaded nanoparticles showed high bioavailability, targeting effect and stability (Lee et al., 2006). Thymoquinone (TQ), derived from the medicinal spice Nigella sativa, has been shown to exhibit anti-inflammatory and anticancer activity (Amin et al., 2009).

Nano-Tablets

The water purification Herbal tablet comprised of nanoparticles that can be used by developing world communities with no access to clean drinking water. This tablet is made with the help of Brahmi (Bacopamonniera) extract on a small ceramic disk filled with silver or copper nanoparticles that is placed inside a water vessel, where it can repeatedly disinfect water for up to six months. NanotABLETS loaded with ayurvedic drugs are used for controlled and targeted delivery. The ayurvedic bhasmas coated nanotABLETS are studied for the anticancer activity. The formulations in the word 'bhasma' have nano particles in them. It is very surprise for many researchers that 5000 year old indian medical system had the knowledge of nano science and technology. Charakasamhitha is the oldest classical way of ayurveda with the concept of reduction in particle size of metals. The bhasmas are used for treatments of various diseases in ayurveda for the past several centuries of years in the form of nanotechnology, some of the common properties in the ayurvedic bhasmas are 'rasayana' (immune modulation and anti agingquality) and 'yogavahi' (ability of drug carry and targeting drug delivery). They were prescribed in minute dosage (15-250mg/day) (Sarkar et al., 2010).

The Nano Coffee energy tablets used for the production of energy drink very easily. The list of active ingredients including vitamin C, niacin, Vitamin B6 B12 B5, Folate, Chromium, Guarana seed extract, caffeine (from natural sources), glucuronolactone, Columbian roasted coffee bean, Taurine, and green tea leaf extract (Nune et al., 2009).

Nanogels

Herbal nanogels are the hydrogel nanoparticles with diameters in the range of 10-100 nm and these nanogels had proved to be more efficient in controlled and targeted drug release. Ayurvedic nanogels are the most effective remedy for our health especially for our heart care. It is the fastest and safest way to lose our weight with no side effects, reduces the fats on abdomen, arms, legs, thighs and double chin. And even it helps for heart tonic, usefull in all heart ailments (Alexander et al., 2009). The nanogels are made up of biopolymers with herbal drugs like curcumin and natural extracts of Caffeine, Laminaria and Ivy. This nano gel travel deeply into the skin and act directly on the extra deposited fat and reduces the extra intracellular water. So the body weight can be reduced with the help of the nanogels. The absorption of water is due to the presence of hydrophilic groups such as ether, sulphate, hydroxyl and carboxyl groups which are present in these gels. They also used on the belly, thighs, breasts, and other areas for reducing the fat. And it also helps to eliminate the harmful material from blood. By this way the digestive power and fat metabolism of body is improved (Mei et al., 2005).
The Boswelliaserrata gum nanogel has been widely used in ayurvedic and traditional medicine for the treatment of inflammation. The nanogel of 3-acetyl-11-keto-β-boswellic acid is used for the anti-inflammatory and anti-arthritic activity. Recently the studies are conducted in the nanogels with ayurvedic combinations for the treatment of Type I diabetics (Kimmatkar et al., 2003).

**Nanoemulsions**

The properties of nano emulsions depend not only on composition but also on the preparation method. About 20 years back, nano emulsions were developed mainly for nano particle preparation, the applications of nanoemulsions are being developed mainly in pharmacy and cosmetics. The ayurvedic nano emulsions with a diameter about 20-200nm are extremely versatile. They were useful in transdermal delivery systems and they are not harmful and non irritant. These nanoemulsions are useful in delivering drugs to cell culture, cancer therapy and as disinfectants. So they increases the solubility and bioavailability of the drug.

Nanoemulsion of caffeine (1, 3, 7-trimethylxanthine), found in tea leaves, coffee, cocoa, guarana, and kola nuts, has been widely studied and has tremendous potential, since caffeine could protect the skin from ultraviolet light-induced skin cancer (V. Mailander and K.Landfester, 2009).

**Nano Paste and Nano Pure (Nano-Air Purification)**

Herbal Nanopaste made up of Aloe Vera is recently studied for the treatment of osteoporosis. This Nanopaste gives strengthen to the bones after surgery and also will have a long-lasting effect since the nanoparticles are released successively and thus continuously stimulate the surrounding bone cells (M.Takahashi et al., 2009)

Nanotechnology has the potential to contribute to long-term air quality, availability, and viability of air resources, such as through advanced filtration that enables more air re-use, recycling, and purification with the help of herbal drugs (Alexander et al., 2006).

**CONCLUSIONS**

Nanophytomedicine is the new trend in the health care research. The Ayurvedic nano medicines are the dietary supplements to maintain good health and they are sold as nanotablets, nanocapsules, nano powder, nanogels, nano paste and nanoemulsions. Recent studies and research on nanoparticles evidenced that in a number of crops germination, physiological activities, nitrogen metabolism, mRNA expression and also positive changes in gene expression indicating their potential for the improvement of herbal plants. The using the nanophytomedicine increases the potential for the treatment of various chronic diseases to provide health benefits. And also the natural nanomedicines will enhance the significance of existing drug delivery systems.

**ACKNOWLEDGEMENTS**

The authors are grateful to Department of Biotechnology(DBT), Government of India for giving support for the study.

**REFERENCES**


APPENDICES

Table 1: Different Nanophytomedicine Formulations and their Biological Activities

<table>
<thead>
<tr>
<th>Formulations</th>
<th>Ingredients</th>
<th>Biological Activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Artemisinnanocapsules</td>
<td>Artemisinin</td>
<td>Anti-cancer</td>
</tr>
<tr>
<td>Curcumin nanoparticles</td>
<td>curcumin</td>
<td>Anti-cancer and Anti-oxidant</td>
</tr>
<tr>
<td>Berberine nanoparticles</td>
<td>Berberine</td>
<td>Anti-neoplastic</td>
</tr>
<tr>
<td>Quercitrin nanoparticles</td>
<td>Quercitrin</td>
<td>Anti-oxidant</td>
</tr>
<tr>
<td>Hypocrellins nanoparticles</td>
<td>Hypocrellins</td>
<td>Antiviral activity</td>
</tr>
<tr>
<td>Ginseng nanoparticles</td>
<td>Ginseng</td>
<td>Antioxidant activity</td>
</tr>
<tr>
<td>Radix salvia nanoparticles</td>
<td>Radix salvia</td>
<td>Anti-angina activity</td>
</tr>
<tr>
<td>Silybin nanoparticles</td>
<td>Silybin</td>
<td>Anti-hepatotoxic activity</td>
</tr>
<tr>
<td>Paclitaxel nanoparticles</td>
<td>Paclitaxel</td>
<td>Anti-tumour activity</td>
</tr>
<tr>
<td>Matrine nanoemulsions</td>
<td>Matrine</td>
<td>Antibacterial, anti-inflammatory</td>
</tr>
<tr>
<td>Rhubarbnanoemulsions</td>
<td>Rhubarb</td>
<td>Cathartic and laxative activity</td>
</tr>
<tr>
<td>Docetaxel nanoemulsions</td>
<td>Docetaxel</td>
<td>Anticancer activity</td>
</tr>
<tr>
<td>Curcuminoids anoparticles</td>
<td>Curcuminoids</td>
<td>Anti-malarial</td>
</tr>
<tr>
<td>Nux vomica Nanogels</td>
<td>Nux vomica</td>
<td>Anti-tumour, analgesic and anti-inflammatory</td>
</tr>
<tr>
<td>Sophora Alopecuroides nanotablets</td>
<td>Sophora Alopecuroides</td>
<td>Anti-endotoxic, anti-cancer and anti-inflammatory</td>
</tr>
</tbody>
</table>

Figure 1: Nanophytomedicine
Figure 2: Nanophytomedical Drug Formulations