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DEVELOPMENT OF HERBAL NANOPARTICLES PRODUCT IN CANCER TREATMENT

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Abstract

Nanotechnology is widely used by experts in the fields of chemistry and medicine that has been allowed to work on the molecular and cellular level. The use of nanoparticles has great advantages resulting from the size and unique physicochemical properties. In recent years, nanotechnology started to grow in the fields of engineering, medicine, electronics, optical and biomedical. Moreover, research and development of engineered multifunctional nanoparticles as pharmaceutical drug carriers have spurred exponential growth in medical applications in the past decade. Nanoparticles design principles including nano-emulsions, dendrimers, nano-gold, and liposomes. This paper will discuss the development of herbal nanoparticles product in cancer treatment.

Key words: *nanoparticles herbal; cancer treatment*

Introduction

Nanotechnology is the study of particles in the size range 1-1000 nm. Nanotechnology is widely used by experts in the fields of chemistry and medicine making it possible to work on the molecular and cellular level. In recent years, nanotechnology started to grow in the fields of engineering, medicine, electronics, optical and biomedical (Stern and Mc Neil, 2008). In the field of pharmaceutical and medical, nanotechnology development has been achieved and applied in human life. One topic that is now the concern is the drug delivery systems. Nanomedicine is the application of nanotechnology in medicine, especially to cure disease and repair of damaged tissue such as bone, muscle, and nerve. Nanotechnology has been able to manipulate the drug to be able to reach the target with the right dose, including opportunities to overcome severe diseases such as tumor, cancer and HIV. The application of nanotechnology in the pharmaceutical field has many advantages, such as can increase the solubility of the compound, reducing the dose of medication and increase absorption.

The use of nanoparticles has great advantages resulting from the size and unique physicochemical properties. Nanoparticles have a special role in targeted drug delivery in the sense that they have all the advantages of liposomes including the size property. But unlike liposomes, nanoparticles have a long shelf life and can entrap more drugs. Polymeric nanoparticles from biodegradable and biocompatible polymers are good candidates for drug carrier to deliver drugs, because they are expected to be adsorbed in an intact form in the gastrointestinal tract after oral administration (Wu Y, 2005). These drug delivery carriers should

exhibit characteristics that include: capacity for drug association, ability to enhance their physicochemical stability and protection of encapsulated drugs from carrier production to release. Furthermore, in many cases, carriers are expected to regulate the drug release profile, while allowing an intimate contact between molecules and mucosal barriers, contributing to their epithelial permeation (Luppi, 2010).

Several studies have reported the manufacture of nanoparticles, such as by Dustgani (2008) conducted a study on the manufacture of nanoparticles of chitosan as a matrix for dexamethasone. Wu Y. (2005) made the nanoparticles of chitosan as a matrix for glycyrrhizinate. Furthermore, Kim (2006) made the chitosan nanoparticles as retinol matrix. Nanoparticle products derived from natural materials such as curcumin that is used for the treatment of cancer. The purpose of this paper is to describe some of the techniques of making herbal nanoparticles have potential as a cancer drug.

Method of synthesis nanoparticles product

Nanomedicine has developed a variety of nanoparticles for drug delivery systems, such as curcumine or other hydrophobic compounds, which previously was a conundrum for the formulation scientists. These delivery system have gained immense popularity in the last decade because of their potential to improve the therapeutic index of the drug is packaged well to protect them from enzymatic degradation, by changing their pharmacokinetics, reduced toxicity or order controlled release over a longer period of time. According to the National Nanotechnology Initiative (NNI), nanoparticulate of delivery system contain encapsulated, dispersed, adsorbed, or conjugated drugs within a particle size range of 1–100 nm (Bansal SS, 2011).

Nanoparticles can consist of a single constituent material or be a combination of several materials. Nanoparticles in nature often found with the agglomeration of materials with different compositions, while the composition of a single pure material can be easily synthesized by various methods. Based on the chemical and electromagnetic properties, nanoparticles can be dispersed as aerosols, suspension / colloid, or in a state of clumping. For example, magnetic nanoparticles tend to cluster, forming agglomerate, unless they are surface coated with a non-magnetic material, and in a state of agglomerated, nanoparticles can behave as larger particles, depending on the size of the agglomerates (Buzea, et al., 2007).

Drug delivery system is a complex system consisting of at least two components, one of which is the active component. Some of the delivery system has been developed, among others, SNEDDS (Self Nanoemulsion DDS), solid lipid nanoparticle, liposome, micelle, and dendrimer (Re F, 2012). Some of the material used for the synthesis of nanoparticles and its application presented in Table 1.

Table 1. Some of the material used for the synthesis of nanoparticles and its application

Particle class	Materials	Application
Natural materials or derivatives	Chitosan; Dextrane; Gelatine; Alginates; Liposomes; Starch	Drug/Gene delivery
Dendrimers	Branched polymers	Drug delivery
Fullerenes	Carbon based carriers	Photodynamics; Drug delivery
Polymer carriers	Polylactic acid; Poly(cyano)-acrylates; Polyethyleinemine; Block copolymers; Polycapro-lactone	Drug/gene delivery

The synthesis of nanoparticles can use several methods such as ionic gelation method, emulsification methods, and coacervation/ precipitation method, and spray drying method. Some of these methods can be described as follows:

1. Ionic Gelation Method

Ionic gelation method involves connecting a cross between polyelectrolyte in the presence of ion-pair multivalen. Ionic gelation is often followed by polyelectrolyte complexation with polyelectrolyte opposite. Formation the cross connect bond will strengthen the mechanical strength of the particles formed. For example, polysaccharide resulting from the deacetylation of chitin compounds contained in the tribe the polymer can use the ionic gelation technique is chitosan with tripolyphosphate. Chitosan is a linear Crustacean shell such as shrimp, lobster, crabs and so on. Chitosan is one of the most commonly used natural polymers in the production of nanomedicines, because it displays very attractive characteristics for drug delivery and has proved very effective when formulated in a nanoparticulate form. Chitosan has further demonstrated capacity to enhance macromolecules epithelial permeation through transient opening of epithelial tight junctions. In addition chitosan is known to be biocompatible and to exhibit very low toxicity (Luppi et al. 2010).

2. Emulsification methods

One method of emulsification is microencapsulation (Sukha PG, 2002). The microencapsulation process is carried out in non-aqueous medium and at a moderate temperature to avoid any chemical degradation of monocrotophos during the encapsulation process. Microcapsules were characterized by optical microscopy and SEM for particle size and morphology, respectively.

Doxorubicin commonly used in cancer therapy produces undesirable side effects such as cardiotoxicity. To minimize these, attempts have been made to couple the drug with dextran and then to encapsulate this drug conjugate in hydrogel nanoparticles. By encapsulation of the drug conjugate in biodegradable, biocompatible long circulating hydrogel nanoparticles, we further improved the therapeutic efficacy of the conjugate. These results suggest that encapsulation of the conjugate in nanoparticles not only reduces the side effects, but also improves its therapeutic efficacy in the treatment of solid tumors (Mitra, 2001).

3. Coacervation/precipitation method

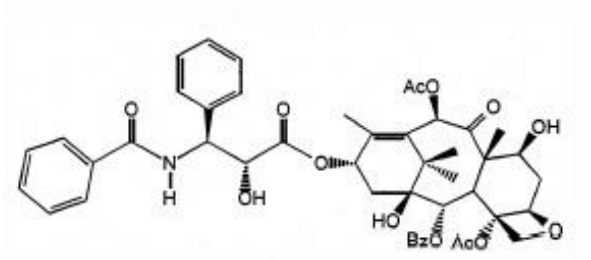
This method is based on the physicochemical properties of chitosan. Chitosan is insoluble in alkaline pH medium, so it can be precipitates when it comes in contact with alkaline solution. Particles produced by blowing chitosan solution in alkaline solution such as sodium hydroxide, NaOH-methanol or ethanediamine using compressed air nozzle to form a coacervate droplets. Further particles separated by filtration/ centrifugation followed by washing successively with hot and cold water. Varying the pressure of compressed air or spray-nozzle diameter is controlled particle size and then use a cross-linking agent to harden the particles can control the release of drugs (Mitra A and Dey B., 2011).

4. **Spray drying method**

In this method, chitosan is first dissolved in aqueous acetic acid solution, drug is then dissolved or dispersed in the solution and then, a suitable cross-linking agent is added. This solution or dispersion is then atomized in a stream of hot air. Atomization leads to the formation of small droplets, from which solvent evaporates instantaneously leading to the formation of free flowing particles. Various process parameters are to be controlled to get the desired size of particles. Particle size depends upon the size of nozzle, spray flow rate, atomization pressure, inlet air temperature and extent of cross-linking (Mitra A and Dey B., 2011). Non-crosslinked and cross linked chitosan microspheres were prepared by a spray drying method. The microspheres so prepared had a good sphericity and a smooth but distorted surface morphology. The release of model drugs (cimetidine, famotidine and nizatidine) from these microspheres was fast, and accompanied by a burst effect (He P, 1999).

Method of synthesis herbal nanopaticle product and its apllication to the treatment of cancer

Currently, there are several products nanoparticles that have been used for the treatment of cancer that is DOXIL (FDA Approved, February 2005). These products can be used of anti-cancer drug for the treatment of refractory ovarian cancer and AIDS-related Kaposi's sarcoma. First to market the product to incorporate technology STEALTH® consisting of lipid nanoparticles that combine with polyethylene glycol (PEG) coating. This coating helps evade the potential impact of the immune system and enables STEALTH® technology to provide the precise delivery of drugs to disease-specific areas of the body. ABRAXANE (FDA Approved, January 2005) as anti-cancer drug used to treat advanced breast cancer. This product is in the form of albumin-bound paclitaxel with a mean particle size of about 130 nanometers.



Taxol

Curcumin is a compound that is found from the rhizome of *Curcuma* genus of plants, such as *Curcuma zedoria*, *Curcuma mangga* which has cytotoxic activity against several types of cancer cells, currently developed in the form of nanoparticles. Research of Mulik R. (2009) showed curcumin nanoparticles with poly (butyl) cyanoacrylate is more stable to acidic conditions and no damage to the storage up to 6 months. Similary, the research of Tiyaboonchai W. (2007) showed curcuminoids in the form of solid lipid nanoparticles showed better stability properties.

One method of making herbal nanoparticles product is using chitosan as drug delivery material. Chitosan is a natural substance that is not toxic. The method of making nanoparticles of chitosan that is widely used is the ionic gelation method. This method was chosen because the process is simple, do not use organic solvents, and can be controlled easily. The principle of the method is the existence of ionic interactions between the amino groups of positively charged chitosan with negatively charged poly-anion compounds form a three-dimensional network structure. Cross linker poly-anion most widely used is sodium tripolyphosphate, because it is non-toxic and has a multivalent. The process is not only the physical cross avoid the use of organic solvents, but also prevent the possibility of damage to the active ingredient to be packaged as a product of chitosan nanoparticles.

Making herbal nanoparticles using chitosan as drug delivery materials can be performed by the method of Wu (2005). Plant tissue used for drug first extracted using ethanol. Extracts were then concentrated. Concentrated extract is then added with 2% chitosan solution and diluted with distilled water. The mixture is then added with 0.1% Sodium tripolyphosphat while stirring continuously. Herbal chitosan nanoparticles were then separated by centrifugation and dried by freeze dryer. Furthermore, herbal products nanoparticles analyzed the physical and chemical properties, particle size, surface structure, and shape of the particles. Such products also need to be tested pharmacological activity, preclinical testing and clinical trials. Research needs to complete before the product is used as a medicine.

Conclusion and Suggestion

Manufacture of herbal products nanoparticles can be made simple and can be done in the laboratory. Nanoparticles of herbal will have a better solubility in the cells of an organism,

reducing the dose of medication, and improve absorption. Research of development nanoparticles product needs to be done in a sustainable manner, so as to produce a cure for cancer useful, safe, and reasonably priced for patients.

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