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(RESEARCH ARTICLE)

Some studies on preparation and evaluation of microspheres containing homeopathic mother tincture of Nux-Vomica seeds

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Abstract

The present study is aimed to investigate the effect of alcoholic mother tincture of Nux-vomica on Peptic ulcer patients with converting the tincture in microspheres. The seeds of Nux-vomica were purchased from local market and identified by University taxonomist Jaipur for authentication purpose. Using standard procedures as mentioned in text mother tincture was prepared and converted to dry powder form. This was further subjected to produce microspheres. Further the evaluations of microspheres were done by physico-chemical methods such as percentage yield, particle size analysis, bulk density, angle of repose and particle shape analysis. The results indicated that the ethanolic mother tincture of *Strychnos nuxvomica* Linn. Family Loganiaceae produced a significant and sustained quality of microspheres which can be used to enhance bioavailability and fast release to small and large intestine inner cell lining and will help in treatment of peptic ulcer, stomach ache and constipation in chronic cases.

Keywords: *Strychnos nuxvomica*; Nux-vomica; Peptic ulcer; Mother tincture; Sustained release dosage form

1. Introduction

The term microcapsule is defined as a spherical particle with size varying from 2 mm to 50 mm, containing a core substance. Microspheres are in strict sense, spherical empty particles. However the term microcapsules and microspheres are often used synonymously. In addition some related terms are used as well. The Microspheres are characteristically free flowing powders consisting of proteins or synthetic polymers, which are biodegradable in nature, and ideally having particle size less than 200 µm. Solid biodegradable microspheres incorporating a drug dispersed or dissolved throughout particle matrix have the potential for control release of drug [1]. On the basis of property microspheres are classified as like density, porosity, and their diameters. Some types of metal microspheres like Al_2O_3, SiO_2 and wax microspheres are as follows 1) Free flowing 2) High precision 3) Embedded agent 4) Coated 5) High porosity 6) High density 7) Precisely fitting diameters 8) Activated doped. A number of different substances both biodegradable as well as non-biodegradable have been investigated for the preparation of microspheres. These materials include the polymers of natural and synthetic origin and also modified natural substances. Synthetic polymers example Acrolin, Epoxy polymers, Ployunhydrides and Natural polymers Gelatin, Chitosan, Polydextran, Albumin, DEAE cellulose.Before preparation of microspheres following some formulation and technology related factors need to consider in detail. The particle size requirement the drug or protein should not be adversely affected by the process. Please ensure reproducibility of release profile and method with no any stability problem. There should be no toxic products associated with final product. Methods of microsphere preparation are as follows. 1)

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Single emulsion technique 2) Double emulsion technique 3) Polymerization techniques a) Normal polymerization b) Interfacial polymerization 4) Phase separation Coacervation technique 5) Spray Drying & spray congealing 6) Solvent Extraction 7) The Brace process [2].

Micro particulate carrier system can be administered through different routes such as intravenous, ocular, intra muscular, intra-arterial, oral etc. Each route has its own biological significance, limitation and pharmaceutical feasibility. Through different routes different mechanisms of uptake, transport and fate of translocation particles have been proposed. Biodegradable micro particulate carriers are of interest for oral delivery of drugs to improve the bioavailability, to enhance drug absorption, to target particular organ and reduced toxicity, to improve gastric tolerance of gastric irritant to the stomach and as carrier for antigen. The polystyrene microspheres administered orally are reported to be taken up by Peyers patch [5]. The particulate matters gain entry into follicle associated epithelium through Peyers patches. After the uptake of particulate carrier via different mechanism their fate becomes important. Some uptake mechanisms avoid the lysosomal system of the enterocytes. The particles following uptake by enterocytes are transported to the mesenteric lymph, followed by systemic circulation and are subsequently phagocytosized by the Kuffer cells of liver. However, after uptake by enterocytes, some particulate carriers may be taken up into vacuoles and discharged back into gut lumen [3]. The characterisation of the micro particulate carrier is an important stage, which help to design a suitable carrier for protein, drug or antigen delivery. The microspheres have different microstructures, which depend on their method of preparation and conditions during preparation. A number of other parameters are generally evaluated for characterisation of microspheres. Particle size and shape, Electron Spectroscopy for Chemical Analysis, Isoelectric point, Capture Efficiency, Release studies, Angle of contact [4] In vaccine delivery by either improved antigenicity by adjuvant action or modulation of antigen release and Stabilisation of antigen. Other applications are Stability, Antigen release, Microspheres & immune system, Targeting using Micro particulate carriers, Magnetic microspheres, Monoclonal antibodies, Chemo mobilization, Imaging, Microsponges: Topical Porous microspheres, Surface modified microspheres [5].

Nuxvomica is prominently the remedy for many conditions incident to the modern life. The typical nux patient is rather thin, spare, quick, active, nervous and irritable. He does a good deal of mental work; has mental strains and leads a sedentary life, found in prolonged office work, over study and close application to business with its cares and anxieties. This indoor life and mental strain demand for stimulants coffee, wine and he hopes to quit his excitement by indulging in sedative effects of tobacco. Sometime really a victim of seductive drugs like opium. Nux is pre-eminently the male remedy. These conditions will produces an irritable, nervous system, hypersensitive & over impressionable, which nux will do much to soothe and calm. Especially adapted to digestive disturbances, portal congestion and hypochondrical states depending thereon. Nux patients are easily chilled, avoid open air etc. Nux always seems to be out of tune; inharmonious spasmodic action [6]. Botanical source: *Strychnos nuxvomica* Linn Family: Loganiaceae, Synonym: Poison nut, Semen strychnus.

Habitat: India and Malaysia, Colour: Greenish brown, Odour: None, Taste: Intensely Bitter, Shape: Disc shape, Size: 10 to 30 mm in diameter, 4 to 6 mm in thickness. Chemical constituents: nuxvomica seeds contain 1.5 to 5 percent of bitter Indole alkaloids. Chief constituent of nuxvomica is Strychnine and Brucine. Seeds also contain 3 percent of fats. Uses: Bitter stomachic and tonic, CNS stimulant, increase the blood pressure and recommended in certain forms of cardiac failure, stimulates respiratory and cardiovascular system, tincture of nuxvomica is used as gastro intestinal tract stimulant, increase appetite and stimulate peristalsis in chronic constipation. [7].

The objective of present study was to prepare and evaluate microspheres of Nux-Vomica mother tincture with suitable method. These microspheres were administered orally in hard gelatin capsule form to different target patients for its therapeutic efficacy on peptic ulcer, stomatitis, and gastric ulcers etc. disorders of human being.

2. Experimental work

2.1. Preparation of powder material of Nux-Vomica seeds

The seeds of Nux-vomica were purchased from local market and identified by University taxonomist Mrs Sumana Datta Jaipur for authentification purpose. The sample was compared with standard herbarium specimen and voucher specimen was NIMSIOP/CD/17/012 deposited. The seeds of nuxvomica were dried first in oven at 40-45 ˚C. The dried material was then subjected to size reduction to coarse powder using grinder. The dried powder of nuxvomica kept with 95% Ethanol for maceration for three days at room temperature. Then all extract was subjected to drying to powder form used further for preparation of microspheres.

2.2. Preparation of microspores

The microspores were prepared by solvent evaporation technique. Completely dry powder form of Nuxvomica mother tincture used for preparation of microspheres with polymer ethyl cellulose: test drug ratio (1:1. 500 mg) in 10 ml of Acetone. In separate beaker 0.2% solution of Sodium lauryl sulphate (600 mg in 300 ml of distil water). The test drug solution with polymer in surfactant solution drop by drop with constant stirring (speed 1000 to 1200 rpm). Then suspension was allowed to settle at room temperature, filtered and obtained microspheres dried in vacuum desicator overnight and stored at 4˚C in the dark. [8]

Further the evaluations of microspheres were done by physico-chemical methods such as percentage yield, particle size analysis, bulk density, angle of repose and particle shape analysis. [9]

2.3. Formulation in capsule form

The dried microspheres then filled in capsules of suitable size with maintaining dose of 50mg, 100 mg and 150 mg with diluents material starch. These capsules were subjected to polishing with cloth containing little amount of Liquid paraffin. Then orally administered to group of patients containing six males in each group by using following protocol. Clinical committee clearance for this was obtained by NIMS/CC/ IC/ 2018/025.

Table 1 Protocol for administration of microspheres of Nuxvomica mother tincture

Sr. No.	Group		Route of Administration	No of Patients
1	Group I	50 mg microspheres of Nuxvomica	Oral	Six male
2	Group II	100 mg microspheres of Nuxvomica	Oral	Six male
3	Group III	150 mg microspheres of Nuxvomica	Oral	Six male

2.4. Patient diagnostic profiles

1) Laboratory tests for H. pylori: The breath tests for H. pylori were carried out for the patients with chronic peptic ulcer history using radioactive carbon in meals determined in the form of Carbon dioxide.

2) Endoscopy: During endoscopy doctor passes a hollow tube equipped with lenses down your throat and into esophagus, stomach and small intestine of patient. If needed biopsy may also advised after sign of continuous bleeding.

3) Barium meals: Patient supplied with barium meal and scanned under X-rays of upper digestive system to check visible ulcers.

3. Results

3.1. Organoleptic Evaluations of Microspheres

Table 2 Showing comparison of organoleptic evaluations of Nuxvomica mother tincture and microspheres**:**

Sr. No.	Particulars	General characteristics of Microspheres	General characteristics of Nuxvomica Mother Tincture
1	Colour	Off White	Greenish brown
2	Odour	None	Nauseating
3	Taste	Bitter	Intense biter

3.2. Percentage yield of microspheres

Table 3 Showing percentage yield of nuxvomica microspheres obtained

Sr. No.	Mass of microspheres obtained (m)	Wt. of drug (d)	Wt. of polymer(p)	Total wt. of d+p	% yield
1	758 mg	500 mg	500 mg	1000 mg	75.8%

3.3. Bulk density

Table 4 Showing bulk density of nuxvomica microspheres obtained

Sr. No.	Wt. of microspheres(m)	Volume occupied by it (v)	Bulk density
1	0.758 gm	1.3 m1	0.5830
2	0.758 gm	1.1 m1	0.6890
3	0.758 gm	1.3 m1	0.5830

Average = 0.6183

3.4. Angle of repose

The angle of repose is the maximum angle obtained between the height of pile and its radius and the angle of repose of prepared granules was found to be:

Table 5 Showing angle of repose of nuxvomica microspheres obtained

Sr. No.	Height of pile(h)	Radius(r)	0=tan-lh\r
1	1.2 cm	2.5 cm	25˚6
2	1.15 cm	2.6 cm	23˚8
3	1.24 cm	2.56 cm	25˚8

Average = 25.0˚

3.5. Particle shape

The shape of the microspheres was observed under electron microscope and it was found to be spherical. The microspheres were observed under light microscope. Images were captured with the help of a camera fitted at the top of the microscope. Figure 1

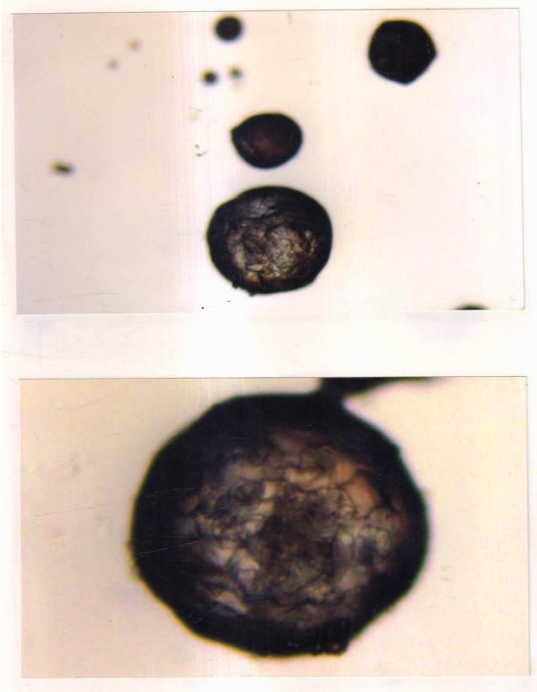

Figure 1 Images of Microspheres containing Nux-vomica

3.6. Particle size analysis

The size of microspheres can be determined with the help of optical microscope. A micrometer scale was fitted in the microscope and the slide of microspheres were prepared and kept on microscope stab and the particle size of randomly selected 10 particles was calculated as:

Table 6 Showing particle size analysis of nuxvomica microspheres obtained

Sr. No.	Particle size (micro meter)
1	24
2	14
3	37
4	19
5	43
6	54
7	22
8	35
9	17
10	57

4. Summary and conclusion

Biodegradability can be tailored to the desired degree by copolymerization of two or more monomers at varying ratios, introducing cross linking between the chains, blending one polymer with the other etc. Attachment of antibodies to spheres loaded with therapeutic agent's offers opportunity to target them to the neoplastic tissue. Recent studies on the uptake of microspheres by Payer's patches have opened up the possibility of delivering many vaccines by the oral route. With the availability of various biodegradable and bio-inspired polymers it shall be now

possible to design microspheres systems for protracted drug release, organ imaging and effective immunization and in development of bio-implantable, bio-reactors, bio-chips, bio-sensors and tissue surrogates prosthesis. The eye and cornea are easily accessible targets and the bioadhesive microspheres are used in intranasal delivery are widely reported. This will help in treatment of peptic ulcer, stomach ache, constipation patients whether chronic or acute. But due to contract and legal restrictions these data not shared here. But significant improvement in patient's health conditions with reduction in elevated enzymes in blood with peptic ulcers and acidity problems treated. This is suggested for future research work in industry. Present work reports suggest that microspheres of dried homeopathic mother tincture of Nux-vomica can be successfully used as microspheres capsule formulation.

Compliance with ethical standards

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Disclosure of conflict of interest

Pande Milind, Hussaini Jibrin and Jha Kishore declare that they have no conflicts to declare.

Statement of ethical approval

The experiments were conducted according to the ethical norms approved by Clinical committee clearance for this was obtained by NIMS/CC/ IC/ 2018/025.

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