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Research Article

HERBAL MICROCAPSULE (A SOLID DISPERSION SYSTEM) DEVELOPMENT AND EVALUATION

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ABSTRACT

The present study was aimed to produce herbal microencapsules using the raw materials obtained from the stolon part of *Glycyrrihiza glabra,* root part of *Hemidesmus indicus,* leaf part of *Aegle marmelos* and the fruit part of *Cuminum cyminum.* With the focus to disperse one or more active ingredients in an inert matrix in the solid state in order to achieve increased dissolution rate, sustained release, improved solubility and stability. The raw materials were authenticated, standardized and individually converted into microcapsule by spray drying technique and micro capsules were evaluated. And the marker component present was quantified by HPLC technique. Qualitative estimation reveals that the formulation does not contain microbes and heavymetals.

Keywords: Spary drying, Microsphere evaluation and HPLC quantification

INTRODUCTION

For many decades, medication of an acute disease or chronic illness has been accomplished by delivering the drugs to the patients via various pharmaceutical dosage forms like tablets, capsules, pills, suppositories, injectable, ointments etc., as carriers. To achieve and then to maintain the concentration of a drug administered within the therapeutically effective range needed for medication, it is often necessary to take conventional dosage forms several times a day which results in a fluctuated drug level, recent technical advances in drug delivery are capable of enhancing the usefulness of medication by controlling the rate of drug delivery, sustaining the duration of therapeutic activity and/or targeting the delivery of drug to a site[1].

The basic concept of microencapsulation was developed during the late 1930's at the National Cash Register Company (NCR) IN Dayton, Ohio. A direct outgrowth of this new technology was the introduction of NCR carbonless paper in 1954. Research continued and resulted in a number of different processes for the encapsulation of micro-particles or micro droplets[2].

- The particle or droplets are dispersed or suspended in an aqueous gelatin solution.
- Several parameters of the dispersion are controlled so as to cause the gelatin to "phase out" of solution forming what is commonly called a "coacervate".
- Under further controlled treatment of the dispersion the gelatin coacervate is deposited onto the particles or droplets.
- Lastly, the capsules dispersion is treated as so to toughen or harden the gelatin capsule wall.

Because of the smallness of the particles, drug moieties can be widely distributed throughout the gastrointestinal tract, thus potentially improving drug sorption. Microencapsulation by spray drying offers the solid liquid as an applicable core material and the approximate particle size of 600µm[3].

MATERIALS AND METHODS

Materials

Stolon part of *Glycyrrihiza glabra,* root part of *Hemidesmus indicus,* leaf part of *Aegle marmelos* and the fruit part of *Cuminum cyminum.* The samples were obtained from Annai Arvind Herbals, Chennai. And the samples were authenticated. All the reagents used were analytical grade.

Raw materials atandardization

As per the WHO guidelines all the raw materials used were standardized for its pharmacognostic and physic-chemical paremeters[4].

Extraction

All the raw materials were initially separated from its foreign matters and pulverised and passed through 18mesh and individually extracted with 60% ethanol solution in the ratio of 1:3 (drug: solvent) three days by cold maceration technique. The extracts were collected and concentrated to one third of its volume.

Development of extract monograph

The obtained extracts were tested for its pH, refractive index, specific gravity, surface tension and viscosity and other organoleptic evaluation also performed[5].

Preparation of microspheres

Concentrated ethanol extract were individually subjected to the technique called spray drying under controlled environmental condition. The ethanolic extracts were homogenized with 12% maltodextrin solution for complete mixing and uniform size distribution. Spray drying involves the dispersing the core material in a liquefied coating material and spraying.

Atomizing the mixture into an air stream the air usually heated which supplies the latent heat of vaporization to remove the solvent from the coating material, thus forming the microencapsulated product. The equipment components of a standard spray dryer include an air heater, atomizer, main spray chamber, blower or fan, cyclone and product collector. Form the product collector the samples were collected. The process produces microcapsules approaching a spherical structure in the size range of 5 to 600 microns[6].

Evaluation of microspheres

Percentage yield of microspheres:

The total amount of microsphere obtained was weighed and the percentage yield was calculated for individual powders[7].

% yield = (Practical yield / Theoretical yield) x100

Micromeritic properties

Bulk and tap density[8] of the prepared microspheres was determined using tap density tester and percentage Carr's index (CI %) Hausner's ratio was calculated. Angle of repose was assessed to know the flowability of wax microspheres, by a fixed funnel method[9].

Morphological analysis

The morphology of the maltodextrin coated microspheres was determined by using F E I Quanta FEG 200 - High Resolution Scanning Electron Microscope**.** The samples were mounted on aluminium stubs using double sided adhesive tape and sputter coated with gold. And the morphological analysis was made at

20.00kv, magnification of 1000x and 1800x at low vacuum mode with WD 9.9mm.

Particle size analysis

Particle size measurements of the maltodextrin coated microspheres were performed at least five times. The particles were analyzed and the average particle size and the particle size distribution range were also determined.

The size of the prepared microcapsules was measured by the optical microscopy method using a calibrated stage micrometer. Particle size was calculated by using equation:

$Xg = 10 \times [(n_i \times \log Xi) / N]$

Where, Xg is geometric mean diameter, n_i is number of particle in range, Xi is the midpoint of range and N is the total number of particles. All the experimental units were analyzed in triplicate (n=3)[10].

Determination of sphericity[11]

To determine the sphericity, the tracings of wax microspheres (magnification 45x) were taken on a black paper using camera lucida (Model-Prism type, Rolex, India) and circulatory factor was calculated by using the equation,

$S = P^2 / (12.56 \times A)$

Where, A – Area (cm^2) and P – Perimeter (cm)

Swelling studies

The swelling behaviour of the maltodextrin coated microsphere was determined. As per the method the dried microsphere were placed in a glass slide and studied under an optical microscope. The image of the microspheres were captured and processed to measure the initial diameter D_0 was noted and a few drops distilled water were dropped over the microspheres for complete immersion and the increase of the swelling diameter D_t was measured as a fraction of time at room temperature. Six microspheres were studied and the swelling ratio Q was calculated by using the following equation.

$Q = [D_t / D_0]$

Where, D_0 – initial diameter; D_t – swelling diameter

Drug entrapment efficiency

Drug entrapment efficiency was calculated by measuring the percentage drug content of marker compound for herbal preparation and the value was divided with the theoretical value and its percentage was calculated[12]. In this study the marker component analysis was carried out by HPLC technique.

$$\text{Entrapment efficiency} = \frac{\text{Estimated \% drug content}}{\text{Theoritical \% drug content}} \times 100$$

The HPLC chromatogram was developed in an instrument called SHIMADZU SPD – 20A containing UV/VIS Detector, using a Column of Phenomenex-5U (Gemini) C18 column, 4.6x250mm size, the mobile phase system used were Methanol: Water [50:50] and 20µl of the samples was flowed at a rate of 0.5ml/min by isocratic technique at the detection wavelength of 205nm the chromatogram was developed using standard Glycyrrhizin.

Determination of wall thickness

Wall thickness of microcapsules was determined by method of Luu et al using equation;

$h = [r (1-P) d1/3\{Pd2+ (1-P) d1\}] \times 100$

Where, h= wall thickness, r = arithmetic mean radius of microcapsules, d1 and d2 are densities of core and coat material respectively, P is the proportion of medicament in microcapsules[13].

Determination of microbial and heavy metals

As per the ayurvedic pharmacopoeia, the prepared microspheres were developed form the herbs it is necessary to test the presence of microbes, Aflatoxins, pesticides and heavy metals.

Short term stability

Short term stability studies were performed over a period of 3 weeks (21days). The microcapsules were packed in screw capped amber colored glass container and kept in hot air oven maintained at 40º±1ºC at ambient humidity condition. Samples were withdrawn at weekly intervals and were examined for physical changes such as color and texture, and assayed for marker compound at the end of third week[7].

RESULTS AND DISCUSSION

Evidance have shown in the recent years that waxy materials have the physical properties and behaviour suitable to prepare gastro resistant, biocompatible, biodegradable microspheres to release the entrapped drug in the intestinal lumen[14].

Authentication: The raw materials used are authenticated authenticated by Prof. P. Jayaraman, Ph.D., National institute of herbal sciences, West Tambaram, Chennai. The voucher no: PARC/2010/658,659,660 and 669.

Standardization of raw materials: As per the ayurvedic pharmacopoeial limits the samples complies ash, extractive values and foreign matter and moisture contents within the limits. Images of the raw materials used were given in the figure 1 – 4.

Extract monograph

From the results it is established that the extracts are slightly alkaline in nature and density of the extract are slightly greater than water; surface tension and viscosity also closer to the range of water and they were viscous enough to spray into the laboratory spray drier. And the value was given in the table 1.

Table: 1 Monograph for ethanol extract of raw materials

Raw material (60% ethanol extract)	pH	Refractive index (º)	Specific gravity (g /ml)	Surface tension (dynes/cm)	Viscosity (centipoise)
Glycyrrhiza glabra	7.51	1.284	1.016g/ml	87.96	0.907
Aegle marmelos	7.3	1.2756	1.044g/ml	91	1.051
Hemidesmus indicus	7.31	1.2588	1.016g/ml	92.51	0.965
Cuminum cyminum	7.5	1.2419	1.016g/ml	78.86	0.947

Note: Tests are performed in triplicate; values are taken as mean± S.E.M

Organoleptic and solubility nature

The obtained microcapsules are creamy yellow in colour, characteristic odor, sweet taste, hygroscopic in nature and freely soluble in water.

Percentage yield of microspheres

Percentage yield of the obtained microspheres was about 75%w/w *Glycyrrhizia glabra* and 66.66% w/w for *Hemidesmus indicus* and 58.33% w/w of *Aegle marmelos* and 41.66% w/w of *Cuminum cyminum*.

Micromeritic properties

Bulk density 0.417 g/cm^3, ture density 0.453 g/cm^3, carr's index 22.3, hausner's ratio 1.27, angle of repose 42º. Tests are performed in triplicate; the results are expressed in Mean ± Standard Deviation. And the angle of repose value lies within the range of 41º – 45º states that passable flow character of powder.

Morphological analysis

The morphological analysis of the microspheres was carried out by light microscopy and scanning electron microsopy (SEM).

Fig 5 and 6: SEM microphotographs showed that the microspheres were spherical in nature, had smooth surface with inward dents and shrinkage, which is due to the collapse of the wall of the microspheres. And it also revealed that the absence of crystals of the drug on the surface of microspheres and uniform distribution of the drug within the microspheres.

Particle size analysis

Particle size distribution was determined using particle size analyzer.

And the size range of the particles lies between 5 - 15µm. Due to smallness of particle size the surface area of absorption increases.

Determination of the sphericity

The sphericity value (circulatory factor) obtained for the microspheres was about 1.00078 which was nearer to the value 1, thus it confirms the sphericity of the microspheres.

Swelling studies

The result of swelling studies was given in table 2. The swelling behaviour of microsphere was performed in distilled water at room temperature. The microsphere absorbs water and increase in diameter at initial and remains constant for next 25 minutes.

Table 2: Swelling behaviour of spheres

Time	0 min	5 min	10 min	15 min	20 min	25 min	30 min
Swelling ratio	0	2	3	3	3	3	3

Quantification of phytoconstituents

Total alkaloid content of microcapsule was found to be about 0.344mg/100g, the total saponin content was about 0.101mg/100g and the volatile oil content was about 0.21% w/w.

Drug entrapment efficiency

The entrapment efficacy of microsphere obtained was determined and the percentage entrapment efficacy was found to be 83.11% w/w. The percentage of drug entrapped is greater in the maltodextrin coat under spray drying technique. HPLC finger print of standard and microcapsule was given in the figure 7 and 8.

Determination of wall thickness

The determined wall thickness of the formulated microcapsules was found to be about 18.89 and it was found to be greater protection of the core material by the coat was effected.

Determination of microbial and heavy metals

Sample does not contains total yeast, molds, salmonella, E.coli, staphylococcus aureus and pseudomonas aureginosa, and contains only the 55cfu/g of total bacterial count. Arsenic, cadmium, mercury were found to be nil and lead 0.988ppm free from aflatoxin and pesticide hence it is proven to be safe for human consumption.

Short term stability

Total alkaloid content of microcapsule was found to be about 0.341mg/100g, the total saponin content was about 0.10mg/100g and the volatile oil content was about 0.2% w/w.

The report states that there was no loss in the alkaloid, saponin and volatile oil content of the microcapsule during stability period and retains its potency.

Fig. 1: ***Glycyrrihiza glabra*** (Rhizome)

Fig. 2: ***Hemidesmus indicus*** (Root)

Fig. 3: ***Aegle marmelos*** (Leaves)

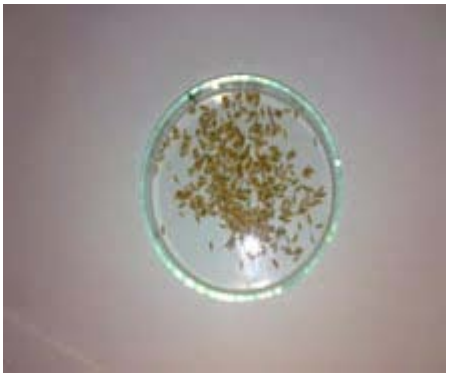

Fig. 4: ***Cuminum cyminum*** (seed)

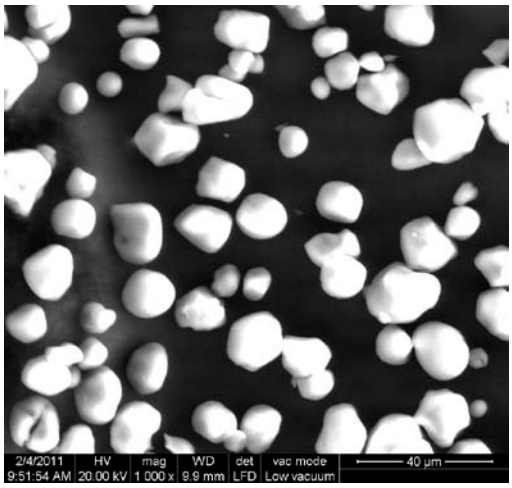

Fig. 5: Microspheres magnified at 1000X

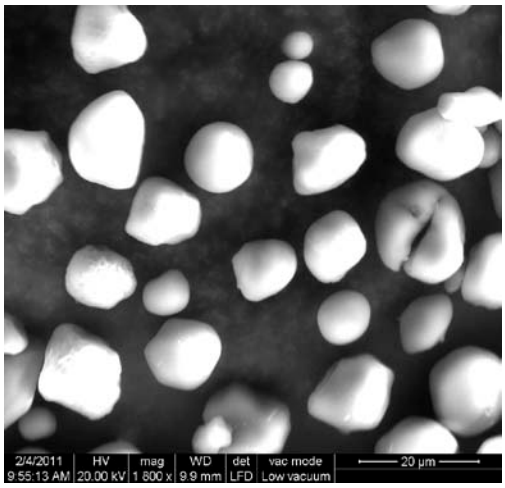

Fig. 6: Microspheres magnified at 1800X

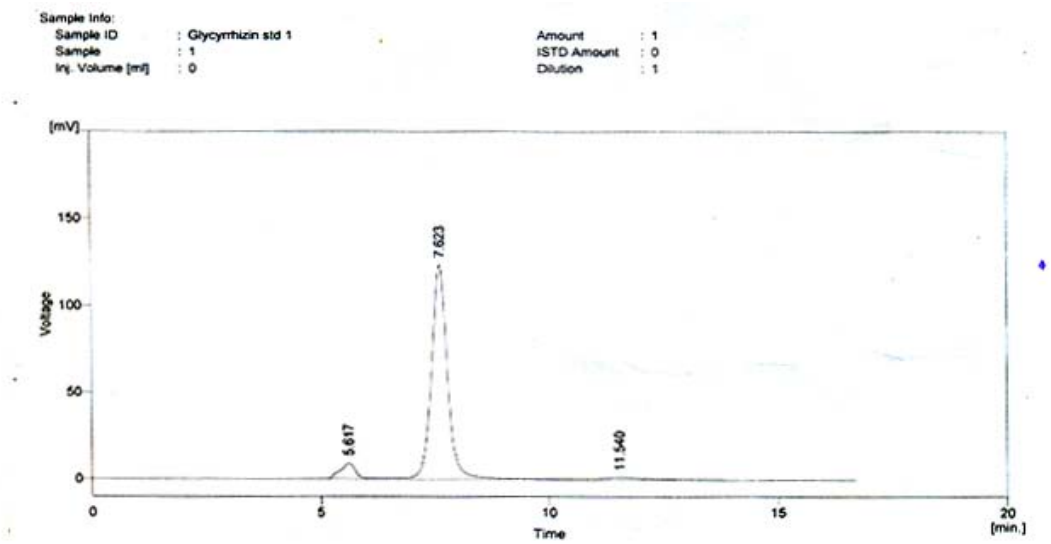

Fig. 7: HPLC finger print of standard marker compound glycyrrhizin at 205nm

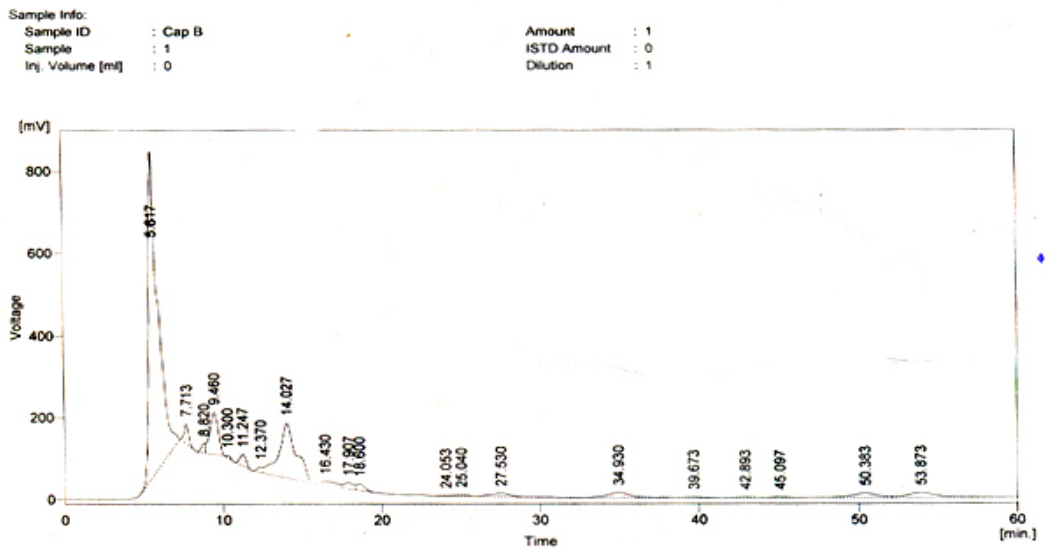

Fig. 8: HPLC finger print of spray dried microcapsules at 205nm

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REFERENCES

1. Martin YC, Kutter E and Austel V. Modern drug research. Volume 12. p 401.
2. Aulton ME, Wells TI. Pharmaceutics: The science of dosage form design. London, England: Churchill Livingstone; 1998. p.647-9.
3. Leon Lachman, Herberty A. Liberman Joseph L Kanig. The theory and practice of Industrial Pharmacy, 3rd ed. 1987. p 427.
4. Quality control methods for medicinal plant materials. WHO Geneva, Indian edition, 2004: 28-37.
5. CVS Subramanyam, J. Thimma setty. Laboratory manual of Physical Pharmaceutics, Edi 2002. p 15.
6. Leon lachman, Herbert A. Liberman, Joseph L. Kanig. The theory and practice of Industrial pharmacy, 3rd ed. 1987. p 426 – 7.
7. Swamy P.V. Hada Amit et al. Preparation and In vitro evaluation of Mucoadhesive Microcapsules of Atenolol. Indian J. Pharm. Res. Oct – Dec 2007; 41(4): 358 – 64.
8. Anonyms. Bulk density and tapped density. In: United states pharmacopoeia. 616. 30th edi.NF -25: The official standard of compendia: 2007.
9. Leon lachman, Herbert A. Liberman, Joseph L. Kanig, The theory and practice of Industrial pharmacy,1987; third edition: 70 – 71 and 183.
10. Gohel MC. et al. Preparation and formulation optimization of sugar crosslinking gelatin microspheres of diclofenac sodium. Indian J. Pharm. Sci. 2005; 67: 575-81.
11. Gowda D.V. Girish B, et al. Preparation and Evaluation of Carnuba Wax Microsphere loaded with Aceclefenac for Controlled Release. Indian J. Pharm. Educ. Res. Oct – Dec 2008; 42(4): 329 – 36.
12. Dhachinamoorthi D, Sangeetha K. et al, preparation and evaluation of Aceclofenac microspheres using emulsion solvent evaporation technique. International Journal of Pharma Research. June – Dec 2008: 25 – 33.
13. Choudary KPR, Rao S. and Rao KN. Influence of solvent and release kinetic on EVA microcapsules of glipizide. The Indian Pharmacist 2007; 57: 73-6.
14. Scchawartz JB, simonelli AP, Highchi WI. Drug release form wax matrices: Analysis of data with first order kinetics and with the diffusion controlled model. J Pharma Sci. 1968; 57: 274-77.