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Formulation and Evalution of Microcapsule Using Novel Polymer as Moringa Oleifera Gum

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ABSTRCT

In the present study the formulation of microcapusle is done with the help of novel polymer such gum *Moringa oleifera*. The gum of moringa has a emulsifying category hence its act as a polymer and the formulation of microcapsule id done using ionic gelation method of microencapsulation. In formulation of microcapsule there are sodium alginate ,moringa gum,calcium chloride for across linking agent. The aceclofenac and ibuprofen are used in formulation. The formulation of micro-capsule is evaluated on various para meter such as Micromeritic studies such as Bulk density, Tapped density, angle of repose, Hausner's ratio, compressibility index for the Gum powder and prepared micro spheres were carried out. Thus using the novel polymer of moringa Gum the controlled release microcapsule is formulated.

Keyword:-Micro-capsule, Moringa Gum, Miceoencapsulation, controlled release, microsperes.

INTRODUCTION

Microencapsulation

Microencapsulation is a process by which solids, liquids or even gases may be enclosed in microscopic particles formation of thin coatings of wall material around the substances.

Applications of microencapsulation

1. The technology has been used widely in the design of controlled release and sustained release dosage forms.
2. To mask the bitter taste of drugs like Paracetamols, Nitrofurantion etc.
3. Many drugs have been microencapsulated to reduce gastric and other G.I tract irritations.
4. Sustained release Aspirin preparations have been reported to cause significantly less G.I. bleeding than conventional preparations.
5. Hygroscopic properties of core material may be reduced by microencapsulation. E.g. Sodium chloride.
6. Microencapsulation has been employed to provide protection to the core materials against atmospheric effects. e.g:Vit.A.Palmitate.
7. Separation of incompatible has been achieved by encapsulation.

Classification of polymers:-

A) Synthetic Polymers: divided into two types;

1) Non-biodegradable- Acrolein, Glycidyl methacrylate, Epoxy polymers, etc.

2) Biodegradable- Polyanhydrides, Polyalkyl cyano acryalates Lactides and glycolides and their copolymers.

B) Natural materials: Obtained from different sources like proteins, carbohydrates and chemically modified carbohydrates.

i) Proteins (albumin, gelatin, collagen)

ii) Carbohydrate (starch, agarose, carrageenan)

iii) Chemically modified carbohydrates [poly (acryl dextran), Poly (acryl starch)]

Advantages of natural gums in pharmaceutical sciences

The following are a number of the advantages of natural plant–based materials.

a. Biodegradable

b. Biocompatible and non-toxic

c. Low cost

d. Environmental

e. Local availability

Disadvantages of natural gums:

a) Microbial contamination

However, this can be prevented by proper handling and the use of preservatives.

b) Batch to batch variation

c) Uncontrolled rate of hydration

d) Reduced viscosity on storage

Moringa oleifera:-

In this modern era of research and technology this futile search still continues to discover novel herbal drugs and alternate source of nutritional supplements. The softwood-tree '*Moringa oleifera*' of the monogeneric family Moringaceae. Every part of this tree is edible and the leaves, roots, seeds, root-bark, stem-bark and pods have medicinal properties.

Taxonomic position

Moringa is the only genus in the family *Moringa*ceae and *Moringa oleifera* is the most extensively studied and cultivated species.

Kingdom - Plantae

Super kingdom - Tracheobionta

Super division - Spermatophyta

Division - Magnoliophyta

Class - Magnoliopsida

Order - Capparales

Family - Moringaceae

Genus - *Moringa*

Species - *oleifera*

Some common names of *Moringa oleifera:-*

Sr.no	**Language**	**Common names**
1	Latin	*Moringa oleifera*
2	Sanskrit	Subhanjana
3	Hindi	Saguna, Sainjana
4	Punjabi	Sainjana, Soanjana
5	Bengali	Sojne danta
6	Gujarati	Suragavo
7	Marathi	Shevga
8	English	Drumstick tree, Horseradish tree, Ben tree

METHODS OF PREPARATION OF MICROSPHERES:

1. Solvent evaporation method

a) Single emulsion technique

b) Double emulsion technique

2. Coacervation phase separation method

3. Spray drying and spray congealing method

4. Polymerization methods

a) Normal Polymerization

b) Interfacial Polymerization

c) Suspension polymerization

5. Wet inversion technique

7. Thermal cross linking

8. Glutaraldehyde cross linking

9. Hot melt microencapsulation

DRUG PROFILE:-

Drug name : Aceclofenac

Chemical name : [[[2-[(2, 6-Dichlorophenyl) amino] phenyl] acetyl] oxy] acetic acid.

Synonym : Aceclofenaco,Aceclofenacum,aceclofenakas

CAS number : 89796-99-6

Mol.formula : C16H13Cl2NO4

Mol.weight : 354.2

Melting point : 149° to 150° C

Origin of substance : Synthetic

Structure :

Category : Non Steroidal Anti-Inflammatory Drug

Solubility : It is practically insoluble in water, soluble in alcohol, freely soluble in Acetone and dimethyl formamide.

Proprietary names : Airtal, Barcan, Biofenac, Difucrem, Falcol, Gerbin, Preservex, Sanein.

Ibuprofen:

Chemically, Ibuprofen is described as 2-(4-isobutylphenyl)propionic acid and is a non-steroidal compound, which exhibits high levels of anti-inflammatory, analgesic and antipyretic activities necessary for the effective treatment of rheumatoid arthritis and osteoarthritis.

Ibuprofen was the first member of propionic acid derivatives class and it was introduced in 1969. It is supplied as tablets containing 200, 400, and 600 mg and also 100 mg/ 5 ml suspension.

(IUPAC) name: (*RS*)-2-(4-(2-*methylpropyl) phenyl) propionic acid*

Description: white or almost white colored crystalline powder

Chemical name :2-(4-isobutylphenyl) propionic Acid

Structure:

Molecular formula: C13H18O2

Molecular weight 206.29 g/mol

Melting point:75 - 770C

Functional category Ibuprofen is used for the treatment of mild to moderate pain,

inflammation and fever caused by many and diverse diseases.

Storage conditions Ibuprofen should be stored at room temperature, between 15-

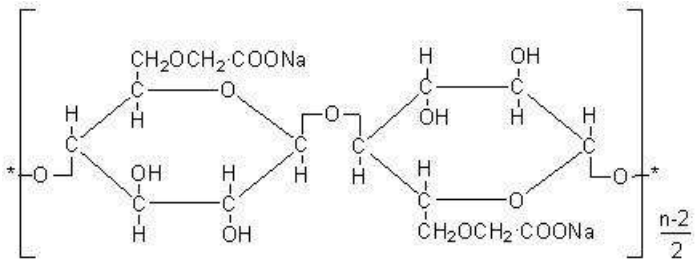
30°C.

Solubility Ibuprofen is very slightly soluble in water (<1 mg/mL) and readily soluble in organic solvents such as ethanol and acetone.

Sodium alginate:

Drug name : Sodium alginate

Chemical structure:



Nature :odourless and tasteless, white to pale yellowish- brown filamentous, grainy, granular or powdered forms.

Chemical name : Sodium alginate

Synonym :align; alginic acid, sodium salt

CAS number :9005-38-3

Mol.formula : (C6H7NaO6)

Mol.weight : 216.121 g/mol

Origin of substance : Synthetic

Category : Stabilizing agent, suspending agent, tablet and capsule disintegrant, tablet

binder, viscosity increasing agent.

Solubility :. It is insoluble in alcohol, hydro-alcoholic solutions with alcohol content

above 30%, chloroform and ether

MATERIALS AND METHODS:-

Sr.no	Chemical	Instruments
1	Ibuprofen	Electronic analytical balance
2	Aceclofenac	UV-Visible spectrometer
3	sodium alginate	Dissolution apparatus
4	Calcium chloride	pH meter
5	HCL	Hot air oven
6		Microscope
7		Thiele's tube apparatus

Pre-formulation studies:

Pre-formulation testing is the first step in the rational development of dosage forms of a drug.

Solubility Analysis:

Pre-formulation solubility analysis was done to select a suitable solvent system to dissolve the drug as well as various excipients used for formulation of microspheres.

Melting Point Determination:

Melting point determination of the obtained drug sample was done as it is a first indication of purity of the sample. The melting point of Aceclofenac and ibuprofen was measured by Thiele's tube apparatus.

Drug excipient compatibility study: A small amount of drug substance with excipient that is, physical mixture of the drug and excipients in ration (1:1) were prepared. A storage period of 2 weeks for 600 c and the sample was retained for 2 months at 400 c. After storage the sample were observed physically for liquification, cracking, odour, or gas forming, discoloration.

Plant material

1) **Collection and drying**

   Gum of required plant were collected of local area. Cleaned and dried at room temperature in shade and away from direct sunlight. The dried gum were powdered in grinder.The fine powdered material was sieved through 60-120 mesh to remove fines and large particles and the powder was subjected for further study.

2) **Authentication**

   The Moringa olirifera Lam. was authenticated at Dept.of Botany and Research centre PVP College, Loni.

3) **Pharmacognostic study**

   The Pharmacognostic study of Moringa olerifera macroscopic, microscopic and physiochemical parameter were studied.

4) Macroscopic Study

   The macroscopic study is morphological description of the plant parts which are seen by eyes or magnifying lens.

Table 5: Formulation of Microcapsule

Formulation	Drug Aceclofenac	Drug Ibuprofen	Sodium alginate	Moringa oliefera gum
F1	**100**	**400**	**500**	**250**
F2	**100**	**400**	**500**	**375**
F3	**100**	**400**	**500**	**500**

Preparation of mucoadhesive microsphere

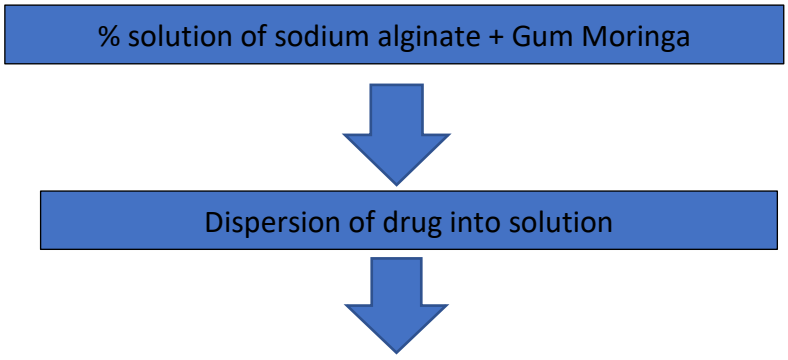
Orifice Ionic Gelation Technique

1) Gliclazide microspheres were prepared by using different ratios of drug: Sod. Alginate: natural gum as mucoadhesive polymer at concentrations (1:1:0.5, 1:1:0.75, 1:1:1) with gum moringa oliefera) and the batches were named as (F1,F2,F3).

2) The pure drug is dispersed in the solution of sodium alginate and water and to this; the gum was added and stirred to get a viscous aqueous dispersion.

3) Drop wisely the dispersion was extruded through 22# syringe needle and poured in 15% c solution by stirring at 50 rpm using a magnetic stirrer.

4) The microspheres thus formed are allowed 30min for curing in calcium chloride solution then were decanted and washed with petroleum ether and air dried over night at room temperature.



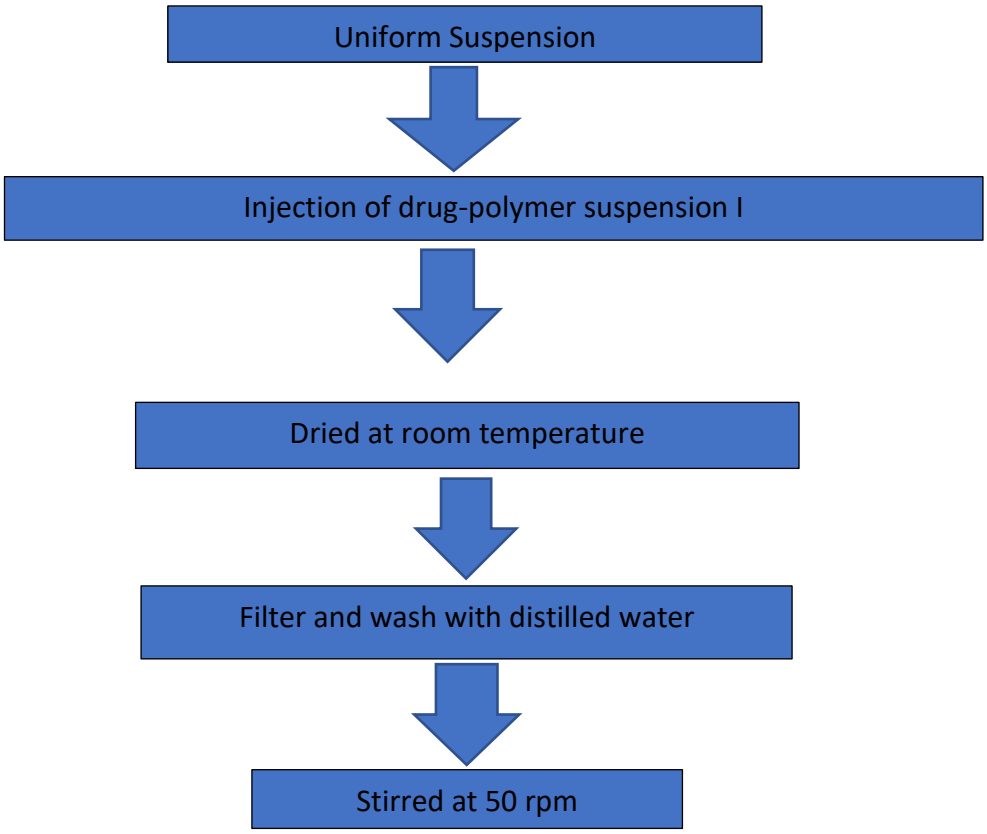


Fig. procedure of microcapsule preparation

Evalution of gum powder and Prepared microsperes

Micromeritic studies such as Bulk density, Tapped density, angle of repose, Hausner's ratio, compressibility index for the Gum powder and prepared microspheres were carried out as follows:

Bulk density:

It is the ratio between mass of microsphere and its bulk volume.

Bulk density = mass of powder/Bulk valume

Bulk density was determined by pouring preserved microspheres into a graduated cylinder via a large funnel and measure the volume and weight.

Tapped Density:

It is the ratio between weight of microsphere and its tapped volume.

Tapped density = Mass of the sample/ Tapped volume

A known weight of the microspheres was transferred to a measuring cylinder, tapped manually 100 times, and the ratio of weight to volume of the microspheres gives the tapped density.

Angle of repose:

Angle of repose was determined using funnel method. The accurately weighed amount of microspheres was taken in a funnel. The sample was allowed to pass through the funnel freely on the surface. Circumference of the pile was drawn without disturbing the pile. The radius was noted as 'r' cm and height was noted as 'h' cm. The angle of repose was calculated by using the following equation.

$\tan \theta = h / r$

Bulk Volume

Mass of the powder

Where,

h = height

r = radius

θ = angle of repose

Relationship between angle of repose (□) and flow properties.

Sr.no	Angle of Repose (degrees)	Flow
1	<25	Excellent
2	25-30	Good
3	30-40	Passable
4	>40	Very poor

Carrs Index

This parameter was computed from tapped (DT) and bulk density (DB) data of the microspheres as in

Carr's index = {(Tapped density – Bulk density)/Tapped density}100

Sr.no	Carr's index %	Flowability
1	5-15	Excellent
2	12-16	good
3	18-21	Fairly acceptable
4	23-35	Poor
5	33-40	Very poor
6	< 40	Very very poor

Hausner's ratio:

Hausner's ratio is one of the parameter to evaluate the flowability of particles. It is not absolute property of the material; its value can vary depending on the methodology used to determine it.

Hausner's ratio can be determined from the formula:

Hausner's ratio = Bulk density /Tapped density

RESULTS & DISCUSSION:-

Organoleptic properties of Gum:-

Organoleptic properties of Gum Moringa Oleifera were found to be as given in following table.

Sr. No.	Organoleptic properties	Result
1.	Colour	Light brown
2.	Nature	Crystalline
3.	Taste	Slightly Bitter
4.	Odour	Odourless

pH determination of Gum:-

pH of gum Moringa found to be 6.

Determination of Solubility:-

The Moringa gum powder is slightly soluble in water and buffer solution.

Determination of Bulk Density, Tapped Density, Hausner Ratio, Carr's Index:-

The data presented here in below table:-

Sr. No	Name of test performed	Results (n=3)
1.	Bulk Density	0.674 ± 0.57
2.	Tapped Density	1.72 ± 0.42
3.	Carr's Index	13.85 ± 0.35
4.	Angle of Repose	30.66 ± 1.45

- **Evaluation of microcapsule:-**

The blended granules of different formulation were evaluated for angle of repose, bulk density, tapped bulk density, compressibility index and Hausner ratio. The results of these evaluations were as follows: -

F.No	Angle of repose	Bulk Density	Tapped Density	Carr's Index	Hausners ratio
F1	30.964±0.04	0.876±0.19	0.589±0.518	12.4±0.22	1.14±0.19
F2	35.73±0.06	0.755±0.528	0.386±0.242	10.68±0.93	4.76±1.22
F3	36.20±1.57	0.589±0.518	0.621±0.226	11.36±1.2	5.01±1.21

1. Angle of repose:-

Angle of repose ranged from 30.9 to 36.20. The results were found to be above 30°C and hence the microcapsules was found to have good flowability. (Table)

2. Loose bulk density and tapped density:-

Bulk and tapped densities are used for the measurement of Compressibility index. (Table)

3. Compressibility index (Carr's index):-

The compressibility index (%) ranged from 5-12. (Table). The blend was found to have excellent flowing property as the result.

4. Hausner ratio:-

The Hausner ratio ranged from 1-5. (Table). The result indicates the free flowing properties of the granules.

- **Invitro Dissolution Test:-**

Drug release was studied by using USP type II dissolution test apparatus in phosphate buffer of pH 6 (900ml). The paddle speed at 100 rpm and bath temperature at 37 ± 0.50 c were maintained throughout the experiment. A sample of micro-capsules equivalent to 500 mg of drug was used in each test.

Sr. No	Time (hr)	F1	F2	F3
1.	1	8.91±0.92	8.97±0.66	9.23±0.99
2.	2	15.2±1.20	29.2±1.90	22.4±0.07
3.	3	39.9±0.98	36.7±0.99	38.7±0.58
4.	4	57.9±0.63	55.2±1.06	46.4±1.8
5.	5	75.5±0.48	82.4±0.98	59.8±0.69
6.	6	93.2±0.89	88±0.35	72.1±1.50
7.	7	94.8±0.42	90.3±0.30	86.5±0.83

The release rate of F3 was found to be higher when compared to other formulations this is due to increase in the concentration of polymer. Drug release from the microcapsules was studied in phosphate buffer of pH 6.8. The release data is given above and . Drug release from the microcapsules was slow and spread over a long period of time and depended on the core: coat ratio and wall thickness of the microcapsules. Drug release from the formulations of F3.

Conclusion

In present investigation an attempt has been made to design and develop Ibuprofen and Aceclofenac controlled release microcapsule using Moringa Oleifera Gum, as release retarding polymers. Ibuprofen and Aceclofenac is widely used as a centrally acting muscle relaxant; therefore have been selected to prepare sustained release dosage forms.An ideal formulation prepared with polymers moringa gum concentrations should release its content in a sustained profile a reasonable length of time.The active pharmaceutical ingredient Ibuprofen and Aceclofenac was evaluated for its physical characteristics, analytical profiles and drug polymer compatibility study. The microcapsules were prepared by Ionic Gelation Technique. The prepared granules were evaluated for Angle of repose, Bulk density, Tapped density and Carr's index. The results obtained were found to be satisfactory and within the specified limits.The investigated Controlled release micro-capsule prepared using novel polymer moringa gum was capable of maintaining constant plasma concentration up to 7 hours. This can be expected to reduced the frequency of administration and decrease the dose dependent side effects. The efficacy and safety of Ibuprofen and Aceclofenac capsule dosage form are expected to offer optimum therapeutic efficacy and improved patient compliance.In the present study the effect and concentration of polymer were studied on In-Vitro drug release. It shows that increase in concentration of

polymer results in the sustained drug release for 10 hours. The study has revealed that by medium concentration of polymer, release rate of drug was retarded and results confirmed that the release rate from capsule depends on concentration of polymer. In present studies, micro-capsule formulation containing Moringa Oleifera Gum is probably showing release up to 93.2± 0.42 within 7 hrs. According to stability study it was found that there was no significant changes in formulatin.

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