Project on development of microcapsule (combination of Diclofenac and Rabeprazole) with a mini Review.

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APPROVAL

This Project, **Project on development of microcapsule (combination of Diclofenac and Rabeprazole) with a mini Review**, submitted to the Department of Pharmacy, Daffodil International University, has been accepted as satisfactory for the partial fulfilment of the requirements for the degree of Bachelor of Pharmacy and approved as to its style and contents.

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Md. Al Fahad Ul Islam (Author)

DEDICATION

I dedicate this work first and foremost to Almighty Allah, then to my parents, to my teachers and my beloved person.

Abstract

Due to its advantages of being biodegradable and biocompatible, polymeric carriers have been widely used in therapeutic drug delivery system formulations. One of the most accepted systems for control release is microencapsulation. This research aims to develop a novel Diclofenac sodium and Rabeparzole combo medication. Also, read several articles to determine which technique is the most effective. The rabeprazole was loaded on the pellets' surface so that it would release quickly and counteract the acid secretion caused by diclofenac. The most often used polymer is HPMC, and the most commonly used technique is ionic gelation, which has the greatest average effectiveness, according to this short review (90 percent). HPMC (3%) and Na-alginate are utilized in this formulation (3 percent). The pellets were brown and sphere-shaped after being loaded with rabeprazole.

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Introduction

1. Introduction

Microencapsulation is a fast growing technique in which very small droplets or particles of liquid or solid substance are encased or coated in a continuous polymeric film [1]. Bungen burg de Jon and Kan (1931) [2] first proposed the microencapsulation technique. Microencapsulation is used to convert liquids to solids, which changes colloidal and surface properties, protects the environment, and regulates the release characteristics of various coated materials[3,4,5]. The majority of microencapsulated products are 1 to 1000 m in diameter [6]. Live cells, adhesives, flavors, agrochemicals, enzymes, medicines, and other essential components may be encapsulated. The structural characteristics of the microencapsulated substance are revealed by scanning electron microscopy [7]. Nanoencapsulation refers to bioactive packing at the nanoscale range and is described as a technique for encapsulating compounds in tiny. The particle size has a direct impact on the transport of any bioactive chemical to different locations inside the body [9,10]. Nanoencapsulation, in comparison to microencapsulation, has the potential to increase bioavailability, improve controlled release, and allow precise targeting of bioactive substances [11]. Nanoparticles are colloidal particles with sizes ranging from 10 to 1,000 nm that may be represented as nano capsules or nanospheres [12]. Nanospheres are matrix systems in which the bioactive chemical is evenly distributed, while nanocapsules are vesicular systems in which the bioactive component is contained to a cavity enclosed by a unique polymer membrane. The efficiency, specificity, and targeting ability of medicinal drugs are all improved by nanoencapsulation [14].

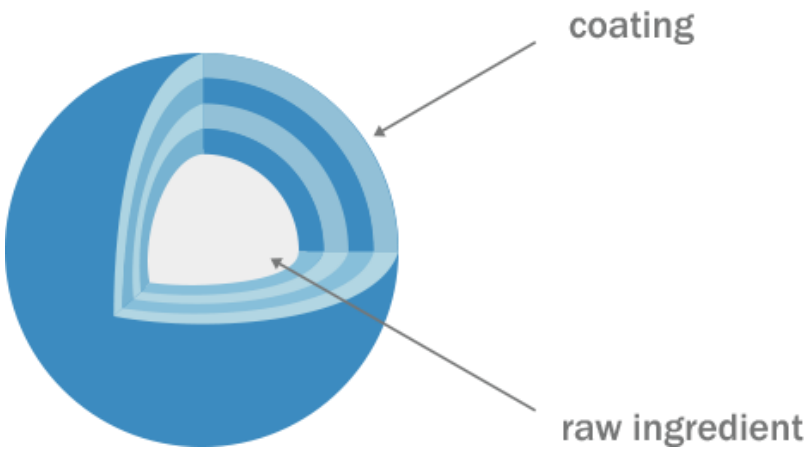

Fig 1: Structure of a microencapsulate [Courtesy Google]

2. Reason for Microencapsulation

Microencapsulation is a technique in which a coating surrounds microscopic particles or droplets to create miniature capsules with beneficial characteristics. In general, it is employed on a micro meter size to integrate food components, enzymes, cells, or other things.

•The most common purpose for microencapsulation is for sustained or extended medication release.

•To enhance patient compliance, this method has been extensively employed to disguise the taste and odor of numerous medicines.

•The liquid medications may be turned into a powder that flows freely.

•Microencapsulation may be used to protect medicines that are susceptible to moisture, light, or oxygen.

• Microencapsulation may help to avoid medication incompatibility.

•Microencapsulation can protect medicines that are volatile and evaporate at normal temperature.

•To decrease toxicity and GI discomfort, several medicines, such as ferrous sulphate and KCl, have been microencapsulated.

Microencapsulation may be used to change the absorption location.

• To alter the absorption location, microencapsulation may be used. This use has shown to be beneficial for medicines with reduced pH toxicity.

• Vitamin A palmitate microencapsulation improves stability and reduces oxidation [15,16].

3. Core Materials for Microencapsulation

The core substance is the material that will be coated, and it may be liquid or solid. The liquid core may include dispersed and/or dissolved components, thus the composition of the core material can be changed. Active components, stabilizers, diluents, excipients, and release-rate retardants or accelerators are all examples of solid core ingredients. The option to change the composition of the core material gives you a lot of freedom, and using this feature enables you to create and develop the microcapsule characteristics you want. The properties of the core material were shown.

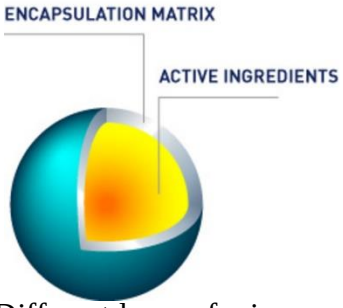

Fig 2: Different layer of microencapsulate

4. Core Materials for Nanoencapsulation

Nanoencapsulation is achieved using core materials such as lipophilic and hydrophilic nutraceuticals. Lipophilic chemicals are water insoluble but soluble in lipids and organic solvents, while hydrophilic compounds are water insoluble but soluble in lipids and organic solvents. Ascorbic acid, polyphenols, and other nanoencapsulated hydrophilic substances 17,18,19,20 Lycopene, beta-carotene, lutein, phytosterols, and docosahexaenoic acid [17,21,22,23] are some of the lipophilic substances that have been nanoencapsulated.

5. Coating Materials for Microencapsulation

The coating material should be able to create a cohesive layer with the core material, be chemically compatible and nonreactive with the core material, and have the required coating characteristics, such as strength, flexibility, impermeability, optical properties, and stability. In situ modification is possible with certain of the coating materials used in microencapsulation techniques. Stabilization of the core material, inertness to active ingredients, controlled release under specific conditions, film formation, pliable, tasteless, stable and non-hygroscopic, low viscosity, and economic, soluble in an aqueous media or solvent, and melting, and the coating should be flexible, brittle, hard, thin, and so on. Coating materials include the following.

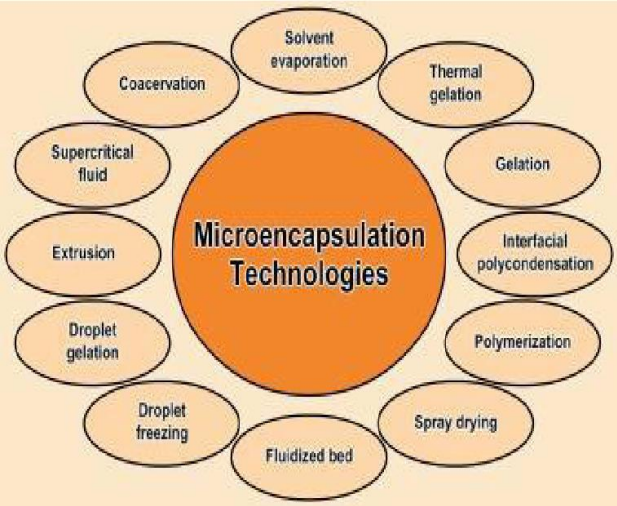

Fig 3: Microencapsulation technology

6. Synthetic polymers

Polymers that aren't biodegradable, such as nylon, are a good example. Acrolein, Glycidyl methacrylate, Polymethyl methacrylate (PMMA), Epoxy polymers [24,25] are a kind of polymer that may be used to make a variety of different things.

Biodegradable polymers, such as polyethylene terephthalate (PET), may be used in a variety of applications Lactides, Glycolides, and Related Polymers [26] Polyalkyl cyanoacrylates are a kind of polyalkyl cyanoacrylate that may Polyanhydrides.

7. Natural polymers

Albumin, gelatin, and collagen are some of the proteins found in the human body [27].

Chemically modified carbohydrates: poly dextran, poly starch [28]. Carbohydrates: agarose, carrageenan, chitosan, starch [28].For Nanoencapsulation, Coating Materials

8. Polymers used in preparation of nanoparticles

The polymers must be adaptable (non-toxic) and non-antigenic, as well as biodegradable and biocompatible with the human body [30].

9. Polymers of nature

Chitosan, Gelatin, Sodium alginate, and Albumin [31] are the most frequently utilized natural polymers in the production of polymeric nanoparticles.

10. Synthetic polymers

Many synthetic polymers exist, such as Polylactides (PLA), Polyglycolides (PGA), Poly(lactide co-glycolides) (PLGA), Polyanhydrides, Polyorthoesters, Polycyanoacrylates, Polycaprolactone, Poly glutamic acid, Poly malic acid, Poly(N-vinyl pyrrolidone), Poly(methyl methacrylate), Poly(vinyl alcohol), Poly(acrylic acid), Poly(acryl)

11. Different Methods of Microencapsulation [32].

11.1 Spray drying

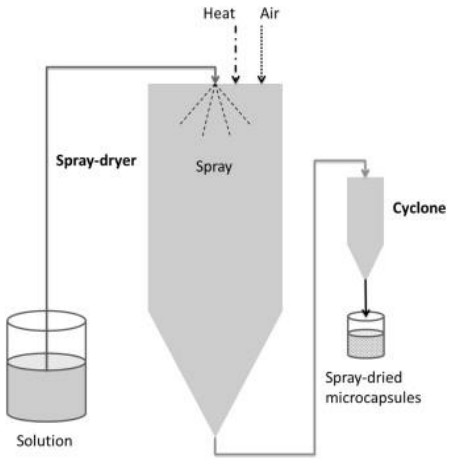

Fig 4: Microencapsulation through Spray drying

Principle

The core material is dispersed in an entrapment substance, then atomized and sprayed into a chamber using a hot air desiccant.

Advantages

a) Low process costs; b) A wide range of coating materials; c) High encapsulation efficiency; d) Good final product stability; e) Large-scale manufacturing in continuous mode is possible.

Disadvantages

a) Can damage extremely temperature-sensitive chemicals; b) Particle size control is challenging; c) Small batch yields are modest.

Spray cooling/chilling

The only difference between spray drying and air desiccant is that the air desiccant is cold.

Advantages

Compounds that are temperature sensitive may be encapsulated.

Disadvantages

a) Particle size management is difficult; b) small batch yields are modest; c) Special handling and storage conditions may be needed.

11.2 Simple extrusion

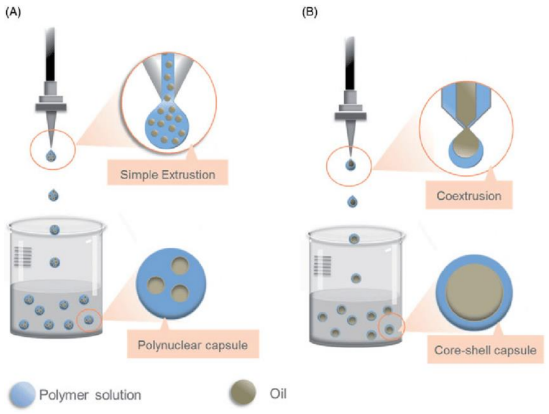

Fig 5: Microencapsulation by simple extrusion

Principle

A core material in a molten wall material mass is forced through a die (laboratory scale) or a set of dies with a chosen cross section into a desiccant liquid bath. When liquids come into touch with the coating material, it hardens and traps the active ingredients.

Advantages

a) The material is completely encased by the wall material; b) Any remaining core is rinsed away from the outside; c) It is a low-temperature entrapment technique.

Disadvantages

a) The capsule must be dried after being removed from the liquid bath; b) Capsules in very viscous carrier material melts are difficult to produce.

11.3 Centrifugal extrusion

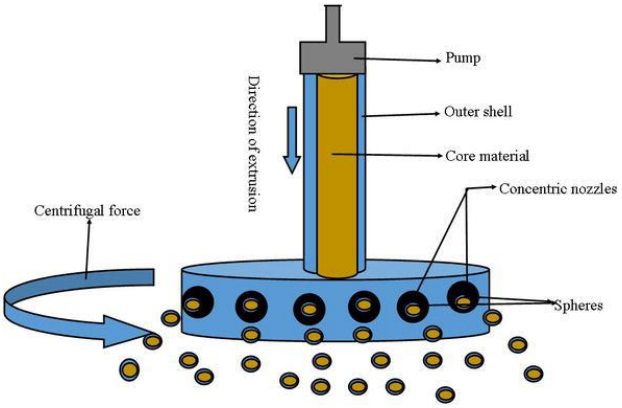

Fig 6: Microencapsulation through centrifugal extrusion

Principle
By centrifugal force, the core and coating materials create a unified jet flow only at the end via a nozzle with a coaxial aperture (coextrusion).

Advantages
The same is true for basic extrusion.

Disadvantages
The same is true for basic extrusion.

11.4 Ionic gelation

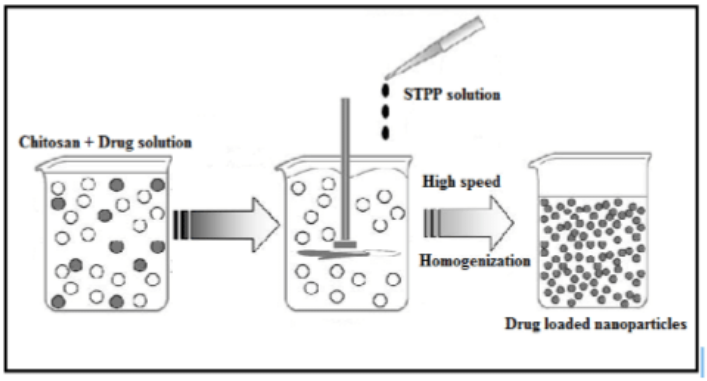

Fig 7: Microencapsulation through Ionic gelation

Principle
Extruded as droplets in an ionic solution, coating material with dissolved core material. Ionic contact causes the capsules to form.

Advantages

Extreme temperatures and pH levels, as well as organic solvents, are avoided.

Disadvantages
a) Generally employed on a laboratory scale; b) Capsules have a high porosity, which encourages intense bursts.

11.5 Thermal gelation

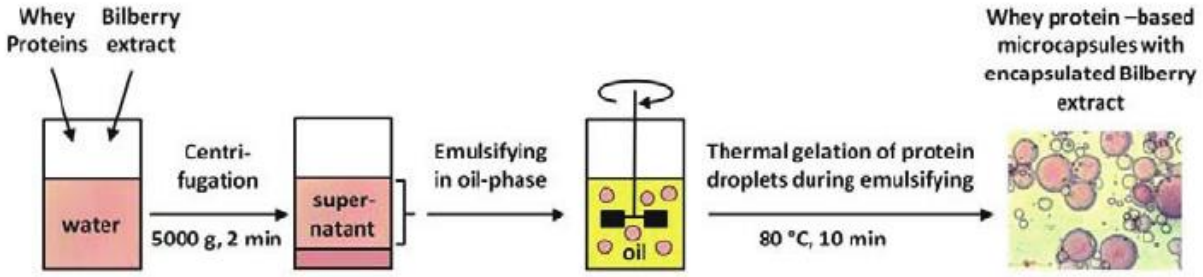

Fig 8: Microencapsulation through thermal gelation

Principle
Although the mechanism is almost identical to that of ionic gelation, there is no need for an ionic solution to produce a gelled drop; the gelation is solely due to temperature factors.

Advantages
a) Ionic gelation b) Ionic gelation c) Fluidized bed coating d) Fluidized bed coating d) This method depends on nozzle spraying the coating material into a fluidized bed of core material in a heated environment.

Disadvantages
It enables precise capsule size distribution and minimal porosities into the product degradation of extremely temperature-sensitive chemicals; a) It is a low-cost process; b) It is a low-cost method.

11.6 Lyophilizaton/ Freeze drying

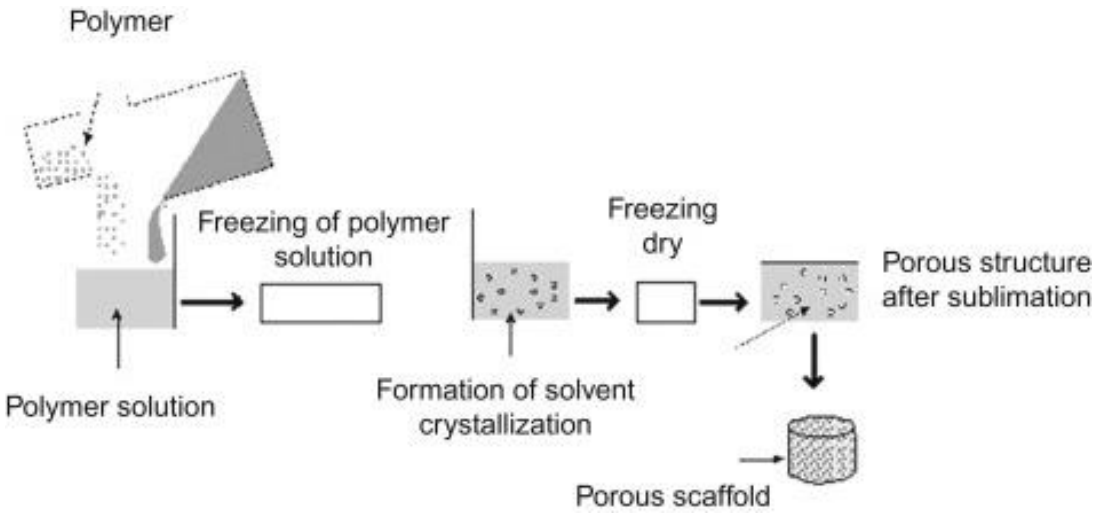

Fig 9: Microencapsulation through freeze drying

Principle
By lyophilizing an emulsion solution comprising a core ingredient and a coating substance, the entrapment is achieved.

Advantages
This method may effectively encapsulate thermosensitive compounds that are unstable in aqueous solutions.

Disadvantages
a) Expensive processing; b) Expensive process expenses; c) Expensive capsule storage and transportation

11.7. Inclusion complexation

Principle
A hydrophobic interaction traps certain apolar molecules within the -Cyclodextrin cavity, where they replace water molecules.

Advantages
a) Effective in protecting b) apolar substances with a high added value, such as tastes

Disadvantages
a) Only apolar molecules with appropriate molecular dimensions may be encapsulated; b) cyclodextrin is costly; c) the generated complex is often released in an undesired manner.

11.8 Emulsion polymerization

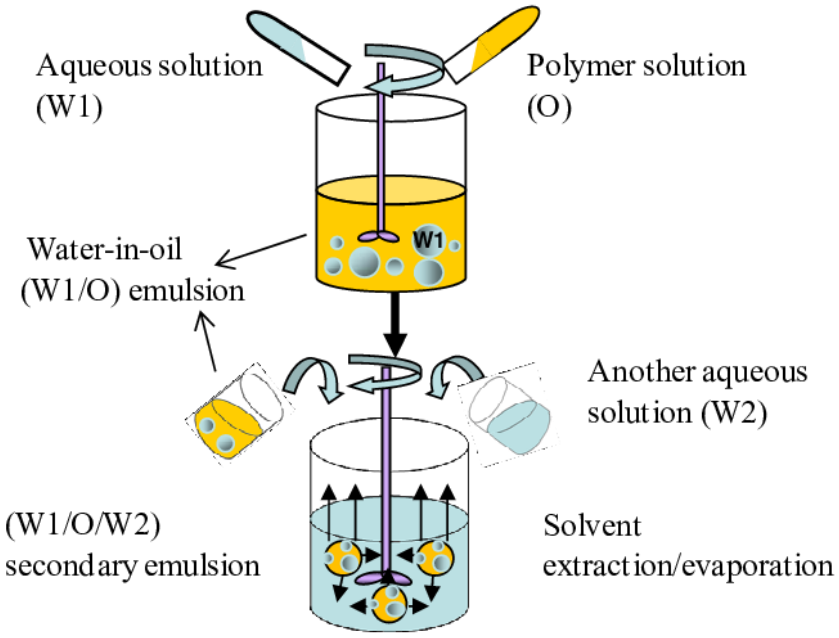

Fig 10: Microencapsulation through emulsion polymerization

Principle
In a polymerization solution, the core ingredient dissolves. In an aqueous solution, the monomers polymerize into capsules.
It is possible to produce micronanocapules with a limited size distribution.

Advantages
a) Capsule formation control is difficult (polymerization) Coacervation
Electrostatic attraction traps the core material by depositing a liquid covering substance around it.
Because it is made at room temperature, it may be used to encapsulate heat-sensitive substances.

Disadvantages
a) Toxic chemical agents are employed; b) Complex coacervates are extremely unstable; c) Residual solvents and coacervating chemicals are present on the capsule surfaces; d) The size range of the spheres is limited; e) The technique is costly and complicated.

11.9. Emulsion Phase Separation

Principle

An oil-in-water emulsion (O/W) or a water-in-oil emulsion (W/O) contains the core material in the polar or apolar layer. A surfactant is used to create the emulsions.

Advantages

a) Emulsions may be polar, non-polar (apolar), or amphiphilic; b) emulsions can be utilized immediately in their "wet" form.

Disadvantages

a) Unstable when subjected to environmental stressors such as heating, drying, and so on; b) Limited number of emulsifiers available.

11.10 Liposome entrapment

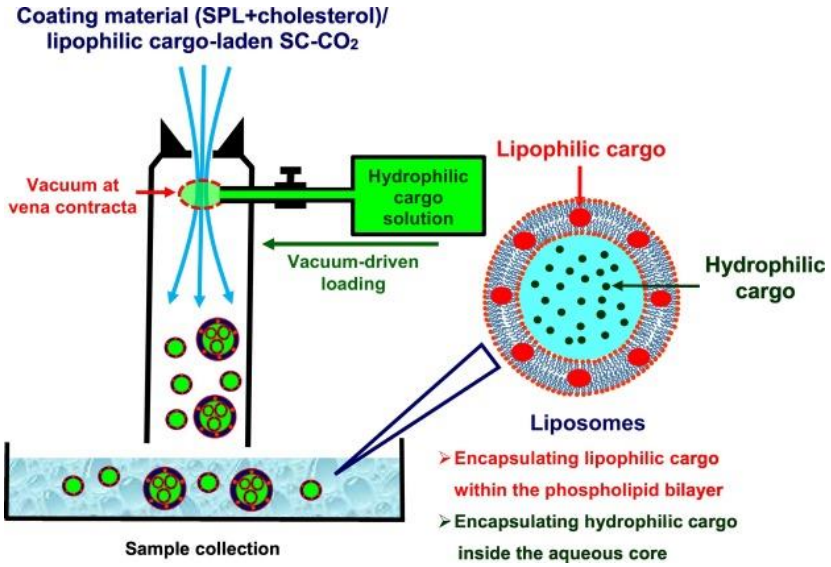

Fig 11: Microencapsulation of liposome entrapment

Principle

Liposomes develop spontaneously when phospholipids are distributed in an aqueous phase. A liposome is used to encase a core substance.

Advantages

a) Aqueous or lipid soluble materials may be encapsulated; b) High water activity applications are possible; c) Efficient controlled administration is possible.

Disadvantages

The majority of the time, it's just utilized in the lab.

12. Coacervation Phase Separation

Three stages are involved in microencapsulation through coacervation phase separation [33]:

• Three immiscible phases form: liquid manufacturing, core material, and coating material.

• Rigidizing the coating, typically by heating, cross bonding, or desolation methods, to create a microcapsule.

13. Extrusion Technique: Centrifugal

A revolving extrusion head with concentric nozzles is used to enclose liquids. A sheath of wall solution or melt encircles a jet of core liquid in this process. The jet breaks up into droplets of core as it travels through the air, each coated with the coating material solution. A solvent may be evaporated from the coating material solution or molten coating material may be hardened while the droplets are in flight. The droplets fall in a tight ring around the spray nozzle because the majority of them are less than 10% of the mean diameter. The capsules may therefore be hardened after creation if necessary by trapping them in a ring-shaped hardening bath16.

14. Spray Drying and Spray Congealing

Spray Drying and Spray Congealing are two different types of spray drying and congealing techniques.

Both spray drying and spray congealing require dispersing the core material in a liquid coating substance and spraying or introducing the core coating combination into an environment where relatively fast solidification of the coating is desired.

Core Material	Characteristic Property	Purpose of Encapsulation	Final Product Form
Acetaminophen	Slightly water soluble solid	Taste-masking	Tablet
Activated Charcoal	Adsorbent	Selective absorption	Dry powder
Aspirin	Slightly water soluble solid	Taste masking, sustained release; reduce gastric irritation; separation of incompatibles	Tablet or capsule
Islet of Langer Hans	Viable cells	Sustained normalization of diabetic condition	Injected
Isosorbide di nitrate	Water soluble solid	Sustained release	Capsule
Liquid crystals	Liquid	Conversion of liquid to solid; stabilization	Flexible film for thermal mapping of anatomy

Menthol/methyl salicylate camphor mixture	Volatile solution	Reduction of volatility; sustained release	Lotion
Progesterone	Slightly water soluble solid	Sustained release	Varied
Potassium chloride	Highly water soluble solid	Reduced gastric irritation	Capsule
Urease	Water soluble enzyme	Perm selectivity of enzyme, substrate and reaction products	Dispersion
Vitamin-A Palmitate	Non-volatile liquid	Stabilization to oxidation	Dry powder

Table 1: Core material and its characteristics

impacted. The manner by which coating solidification is achieved is the primary distinction between the two approaches. The fast evaporation of the solvent in which the coating ingredient is dissolved causes coating solidification in the case of spray application. However, in the spray congealing technique, coating solidification is achieved by thermally congealing a molten coating material or by solidifying the dissolved coating by introducing the coating core material combination into a nonsolvent. Sorption extraction or evaporation methods [34,35] are used to remove the nonsolvent or solvent from the coated product.

15. Method for Pan Coating

One of the oldest industrial processes for producing tiny, coated particles is the pan coating process, which is extensively utilized in the pharmaceutical sector. In a pan, the particles are tossed as the coating substance is slowly applied. Solid particles larger than 600 micrometers are usually regarded necessary for successful coating in microencapsulation. The coating is applied to the required solid core material in the coating pan as a solution or as an atomized spray in practice. Warm air is usually blown over coated objects when coatings are placed in the coating pans to remove the coating solvent. Final solvent elimination is sometimes achieved in a drying oven [36,16].

16. Solvent Evaporation Techniques

In a liquid production vehicle, this method was tested. The microcapsule coating is dissolved in a volatile solvent that cannot be mixed with the liquid production vehicle phase. In the coating polymer solution, a microencapsulating core material is dissolved or distributed. To achieve the suitable size microcapsule, the core coating material combination is disseminated in the liquid production vehicle phase using agitation. The solvent for the polymer is then evaporated by heating the mixture (if required). The polymer solution shrinks around the core when the core material is distributed in it. A matrix - type microcapsule is produced when the core material is dissolved in the coated polymer solution. With continuous agitation, the temperature of the liquid vehicle is lowered to ambient (if needed) after all of the polymer's solvent has been evaporated. The microcapsules may now be utilized in suspension, on substrates, or as powders. A broad range of

liquid and solid core materials may be used to make microcapsules using the solvent evaporation method. Water-soluble or water-insoluble materials may be used as the core materials. Coatings may be made using a number of film-forming polymers [37].

17. Polymerization Process

The technique entails a reaction between a monomeric unit and a continuous phase in which the core material is distributed. The polymerization process takes place at a liquid-liquid, liquid-gas, solid-liquid, or solid-gas interface because the continuous or core material supporting phase is often a liquid or gas [38].

Literature review

2.1. **Methavee Peanparkdee et al, microencapsulation: a review of applications in the food and pharmaceutical industries, Agricultural Science, 4: 56 – 65, 2016**
Microcapsules are now used in a variety of items including beverages, baked goods, meat, poultry, and dairy. Microencapsulation has also been utilized in the pharmaceutical industry to enhance medication stability, conceal harsh taste, improve drug release characteristics, and offer targeted drug delivery. Microencapsulation presents a difficulty in determining the best circumstances for generating highly effective microcapsules. The quality of microcapsules is influenced by a number of variables, including preparation methods, core material kinds, and wall material types.

2.2. N. Venkata Naga Jyothi et al, Microencapsulation techniques, factors influencing encapsulation efficiency, Journal of Microencapsulation, 2010; 27(3): 187–197
Encasing micron-sized particles in a polymeric shell is known as microencapsulation. For the encapsulation of drug entities, several methods are available. The encapsulation effectiveness of a micro particle, microsphere, or microcapsule is determined by a variety of variables such as polymer concentration, polymer solubility in solvent, solvent removal rate, organic solvent solubility in water, and so on.

2.3. **P.Venkatesan et al, MICROENCAPSULATION: A VITAL TECHNIQUE IN NOVEL DRUG DELIVERY SYSTEM, *J. Pharm. Sci. & Res. Vol.1 (4), 2009, 26-35.***
There are many methods for delivering a medicinal material to the target location in a regulated, continuous manner. Microspheres as medication carriers is one such method. Microencapsulation is the technique of surrounding and enclosing tiny discrete solid particles or liquid droplets in an unbroken shell. Microencapsulation is a technique for changing and delaying the release of drugs from pharmaceutical dosage forms. A well-designed controlled drug delivery system may help to overcome some of the drawbacks of traditional treatment while also improving a medication's therapeutic effectiveness. It is a dependable method for delivering the medication to the target location with specificity, if adjusted, and maintaining the appropriate concentration at the place of interest without side effects. Microspheres have gotten a lot of interest recently, not just for their long-term release, but also for their ability to direct anticancer medicines specifically to tumors. The purpose of this article is to show how microencapsulation may be used to deliver new drugs.

2.4. **Nitika Agnihotri et al, Microencapsulation – A Novel Approach in Drug Delivery: A Review, Indo Global Journal of Pharmaceutical Sciences, 2012; 2(1): 1-20**
Microencapsulation Review is a well-established journal dedicated to the preparation, properties, and applications of individually encapsulated novel small particles, as well as significant advancements in tried-and-true techniques relevant to micro and nano particles and their use in a wide range of industrial, engineering, pharmaceutical, biotechnology, and research applications. Its scope includes any other tiny particle systems that need preparative treatment, such as self-assembling structures. The study discusses encapsulation materials, the mechanics of release through the capsule wall and/or desorption from the carrier, preparation methods, and a variety of applications.

2.5. **JYOTHI SRI.S et al, MICROENCAPSULATION: A REVIEW, International Journal of Pharma and Bio Sciences, Vol 3/Issue 1/Jan – Mar 2012.**

The encapsulation effectiveness of microparticles, microspheres, and microcapsules is determined by a variety of variables, including polymer content, solubility in solvent, rate of solvent removal, and solubility of organic solvent in water. A variety of methods are available for microencapsulation. Microencapsulation is a technique for enclosing a substance's core material inside capsule walls for a set amount of time. Alternatively, core components may be enclosed such that they are released either gradually via the capsule walls (known as controlled release or diffusion) or when external circumstances cause the capsule walls to rupture, melt, or dissolve (known as external trigger release). This article examines microencapsulation and the materials used in it, as well as the morphology of microcapsules, microencapsulation technologies, microencapsulation purposes and benefits, release mechanisms, and application fields, with a focus on microencapsulated additives in building construction materials.

2.6. **G Murtaza et al, Microencapsulation of Diclofenac Sodium by Nonsolvent Addition Technique, Tropical Journal of Pharmaceutical Research April 2010; 9 (2): 187-195**

Micromeritics, scanning electron microscopy (SEM), Fourier transform infrared spectroscopy (FTIR), x-ray diffraction (XRD), dissolving test, and heat analysis were used to evaluate the microparticles produced using the non-solvent addition phase separation technique. The microparticles were white in color, irregular in shape, aggregated, and measured between 390 and 442 micrometers in diameter. The effectiveness of drug embedment was 89-91 percent. According to characterization tests, the drug and the polymer in the microparticles did not have a significant chemical interaction. The concentration of polymer and the time it took for it to release was proportionate. Preparing a diclofenac sodium-ethylcellulose multi-unit controlled release drug delivery system using non-solvent addition phase separation is a viable option.

2.7. **M. F. AL-OMRAN et al, Taste masking of diclofenac sodium using Microencapsulation, j. microencapsulation, 2002, vol. 19, no. 1, 45±52**

The wet agglomeration method was used to transform microcrystalline cellulose (Avicel) and lactose powder into spherical cores, which enabled coacervation and the creation of thin and homogeneous microcapsule walls. To give the microcapsules more flexibility, plasticizers such as Diethylphthalate (DEP) and Polyethyleneglycol 600 (PEG) were employed at different percentages (20 and 40% w/w). The microcapsules were compared to a crushed commercially available DS enteric coated tablet to see how much DS they released (Voltaren). A tasting panel of ten participants assessed the microcapsules that had been produced. The ratio of solvent to non-solvent needed for microcapsule production was found to be 1:2. When compared to other microcapsules and crushed commercial enteric coated tablets, microcapsules containing PEG 20 percent or DEP 40 percent exhibited a quicker rate of DS release (Voltaren). Microencapsulation significantly enhanced the palatability and flavor of DS. The microcapsule core:wall ratio, the presence of additives inside the core, the kind and concentration of plasticizer, and the initial core size all had an impact on the degree of flavor masking.

2.8. **K.M. Manjanna et al, Microencapsulation: An Acclaimed Novel Drug-Delivery System for NSAIDs in Arthritis, *Therapeutic Drug Carrier Systems*, 27(6), 501–532 (2010)**
Nonsteroidal anti-inflammatory drugs (NSAIDs) such as aspirin, diclofenac, aceclofenac, ibuprofen, fl urbiprofen, indomethacin, piroxicam, dexibuprofen, ketoprofen, nabumetone, nimesulide, and naproxybenzamide are now used to treat many types of arthritis, including osteoarthritis, However, since the frequent dosage needed by NSAIDs frequently results in patient noncompliance, drug-delivery systems should be developed to decrease dosing frequency and allow for prolonged release of medicines. Microencapsulation is one of the new drug-delivery methods being used to keep drugs on the market for a longer period of time. This technique lowers dosage and eliminates stomach discomfort, resulting in higher patient compliance with arthritis medication. We provide a thorough review of various microencapsulation technologies utilized in the treatment of arthritis that have the potential to decrease the dose-related side effects produced by NSAIDs.

2.9. **Payam Khazael et al, Formulation of Ibuprofen Beads by Ionotropic Gelation, Iranian Journal of Pharmaceutical Research (2008), 7 (3): 163-170**
The only ion that can produce ibuprofen beads is Ca. The beads' appropriate nature is shown by their excellent swelling profile in phosphate buffer (pH=7.4) and absence of swelling in hydrochloric acid (pH=1.2). Furthermore, encapsulation effectiveness of approximately 90% was achieved using a combination of Na-alginate (2%) and Ca-chloride (2%) beads. Ibuprofen was released rapidly and completely from the beads in phosphate buffer medium, particularly those made from Na-alginate (2%) and Ca-chloride (2%). Within the acidic media, however, there was no discernible drug release. To summarize, ibuprofen may be microencapsulated as a bead formulation with acceptable characteristics and a predictable release profile.
2.10. **N. Carreras et al, Drug release system of ibuprofen in PCL microspheres, Colloid and Polymer Science · January 2012**
Microencapsulation of the active principle not only addresses medication ingestion issues, but it also regulates dose. The creation of a protocol for the solvent evaporation technique of microencapsulating ibuprofen was carried out in this research. Following that, the microencapsulates were applied to biofunctional textile substrates (cotton, polyamide, acrylic, and polyester) via a finishing process, and then samples of the treated fabrics were submerged in a thermostatized vessel at semi-infinite temperatures to study the release of active principle in two different media (deionized water and physiological serum). A UV spectrophotometer was used to assess how many active principles were released into the bath. These experimental findings were examined and assessed, allowing a controlled drug release system based on Fickian diffusion in various mediums to be defined.

Purpose of the study

1. The aim of studying microencapsulation is to elevate a new and effective drug delivery system which can reduce toxicity as well as gastrointestinal irritation.

2. This study has created a field for hands-on application of available knowledge about microencapsulation.

3. My aim is to find out the best method for developing microencapsulation

4. Drugs like NASIDs have short elimination half-life and shows severe toxicity when administrated systemically in higher doses. My aim is to overcome this problem.

5. The objective of adding rabeprazole as a combination therapy to inhibit acid (HCL) secretion therefore minimize risk of bleeding or ulcer which can appear for the use of ibuprofen (NSAID) .

6. In the field of microencapsulation there is no such formulation of diclofenac along with Rabeprazole, so my aim is to develop new solid dosages form

Method and material

4.1. Reagents for pelletization:

S.I. No.	Reagents
01.	Sodium Alginate-polymer
02.	HPMC(Hydroxypropyl methylcellulose)-polymer
03.	Water
04.	Calcium Chloride($Cacl_2$)
05	Diclofenac (API)-250mg
06.	Rabeprazole (API)- 250mg

Table 2: Reagents for pelletization

4.2. Apparatus

S.I. No.	Reagents
01.	Weighing balance
02.	Weighing balance
03.	Spatula
04.	Foil papers
05.	Volumetric flasks

06.	Water bottles
07.	Beakers
08.	Filter papers
09.	Stands
10.	Funnels
11.	Glass rod
12.	Water Bath
13.	Syringes-Size 22needles

Table 3: Apparatus

4.3. Pellets formulation

Serial No	Concentration of Diclofenac	Concentration of Rabeprazole	Concentration of sodium alginate	Concentration of HPMC	Calcium Chloride($Cacl_2$)
F-1	5 mg/ml	1 mg/ml	2.5%	2%	3%
F-2	5 mg/ml	1 mg/ml	3%	3%	3%

Table 4: Pellets formulation

4.4. Methods of Pelletization

This formulation as done by to phase. Such as 1. Load of Diclofenac 2. Load of Rabeprazole. In this study I have used ionotropic gelation technique. The technic is given below.

4.4.1. Phase 1:

Load of Diclofenac and Pelletization

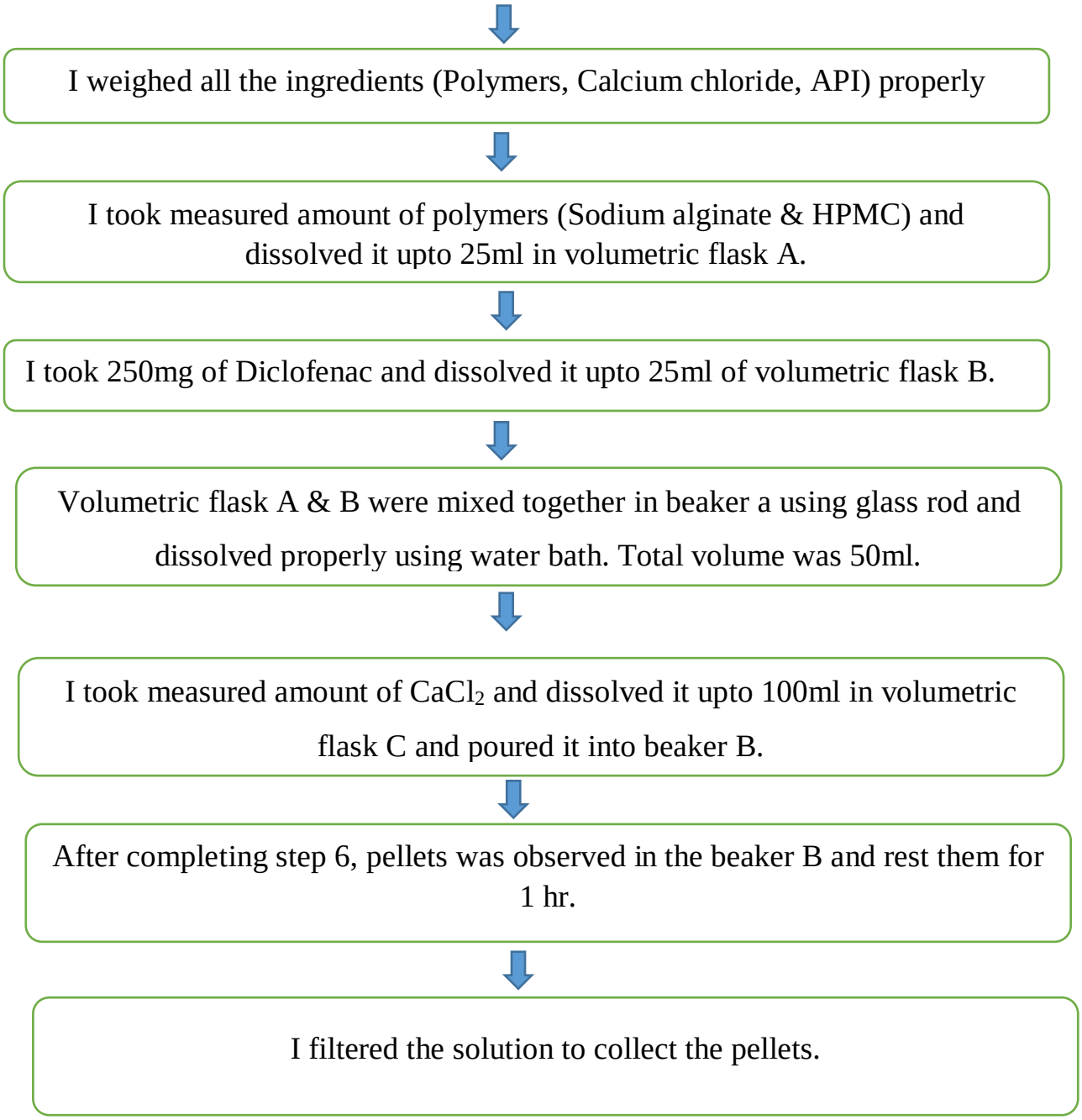

Fig 12: Load of Diclofenac and Pelletization

4.4.2. Phase 2: Load of Rabeprazole

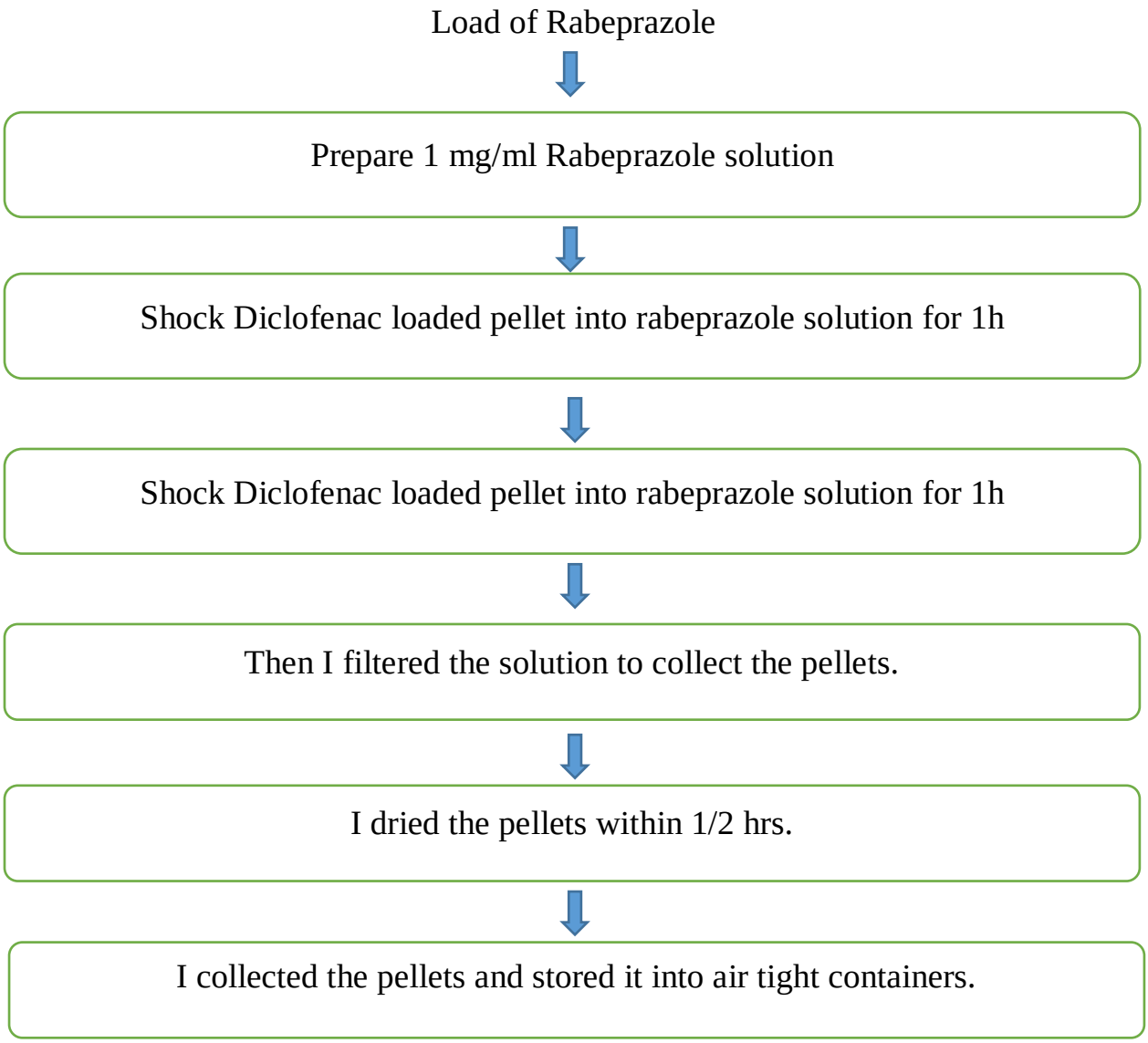

Fig 13: Load of Rabeprazole

4.5. Method of literature review

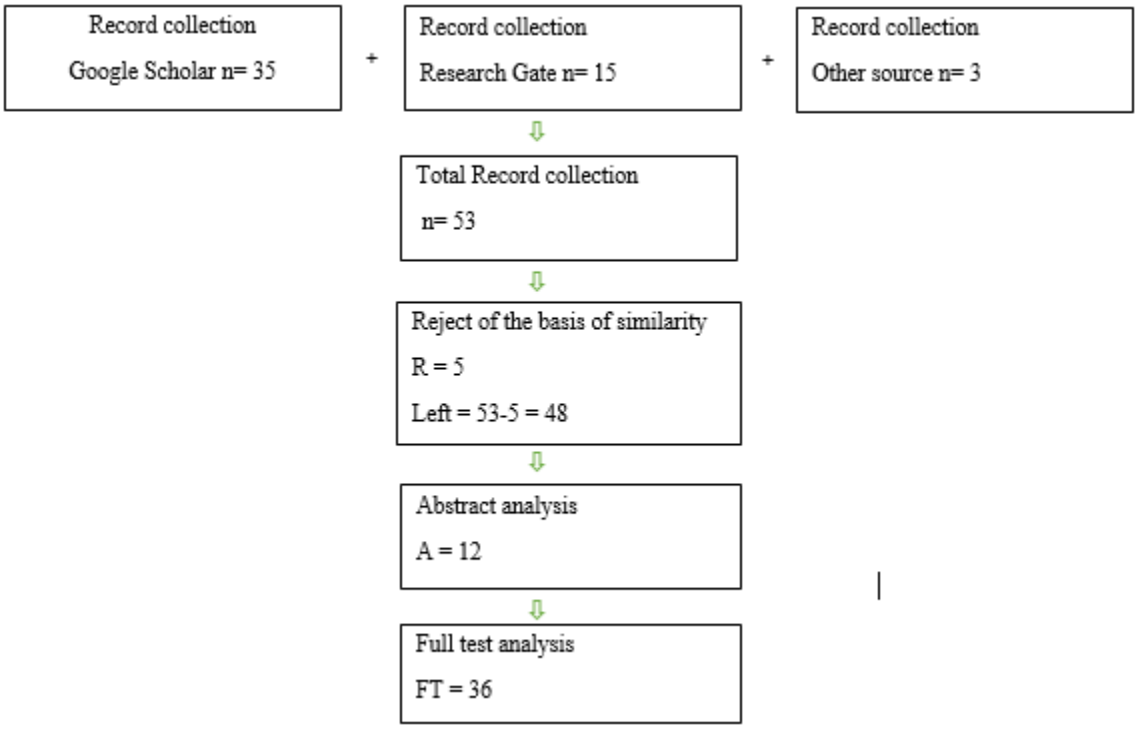

Fig 14: Method of literature review

This study is conducted through reviewing 53 article. At first I Found 35 article in google scholar, 15 in Research gate and 3 in the other source. On the basis of similarity at first I reject 5 (R=5) and 12 articles (R=12) was reviewed only abstract. 36 articles (FT=36) was fully analyzed. The summary of the articles are given below.

Result and discussion

Result on the basis of review

5.1.1 Mostly used polymer

A polymer is a natural or manufactured material made up of big molecules called macromolecules that are multiples of smaller chemical units called monomers. In living creatures, polymers make up a large portion of the components.

Polymer	Used in different formulation n (%)
Ethylcellulose (EC)	3 (13%)
HPMC	5 (21.7%)
Na-alginate	4 (17.4%)
Methylcellulose (MC)	5 (21.7%)
Eudragit	2 (8.7%)
NaCMC	4 (17.4%)

Table 5: Polymer used in different formulation

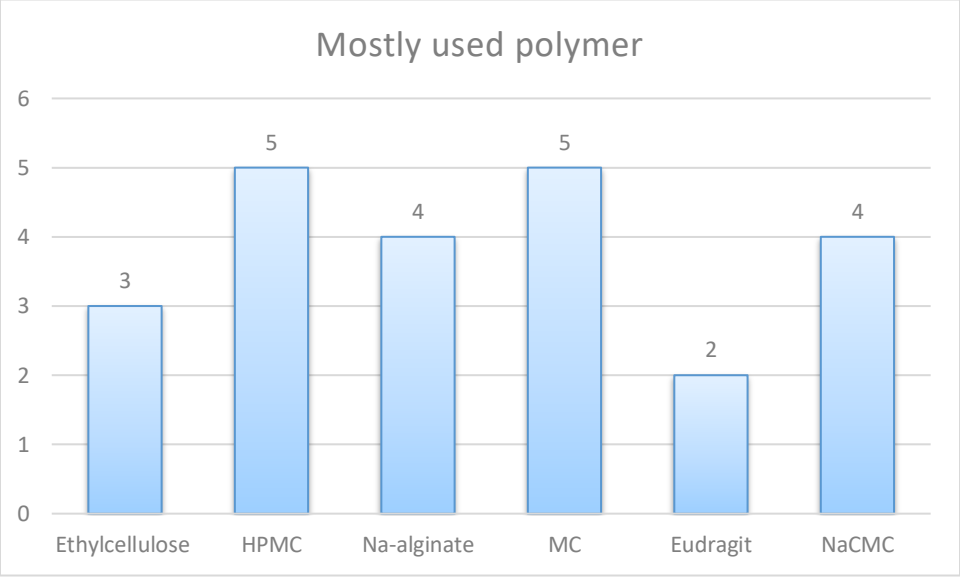

Fig 15: Mostly used polymer

Discussion: There are so many polymer which can be used in microencapsulation. According to this review the mostly used polymer is HPMC and MC. But Na-alginate is a powerful gel forming polymer [39-58]

5.1.2. Mostly used method

In the food and pharmaceutical sectors, microencapsulation is a common method. This method may be used to lower manufacturing costs, enhance compound stability, conceal unpleasant tastes, and improve medicinal component release characteristics.

Method	Used in different formulation n(%)
Non-aqueous emulsion solvent evaporation method	2 (15.38462)
Ionic gelation	5 (38.46154)
Emulsion polymerization	2 (15.38462)
Freeze drying	1 (7.692308)
Thermal gelation	3 (23.07692)

Table 6: Mostly used method

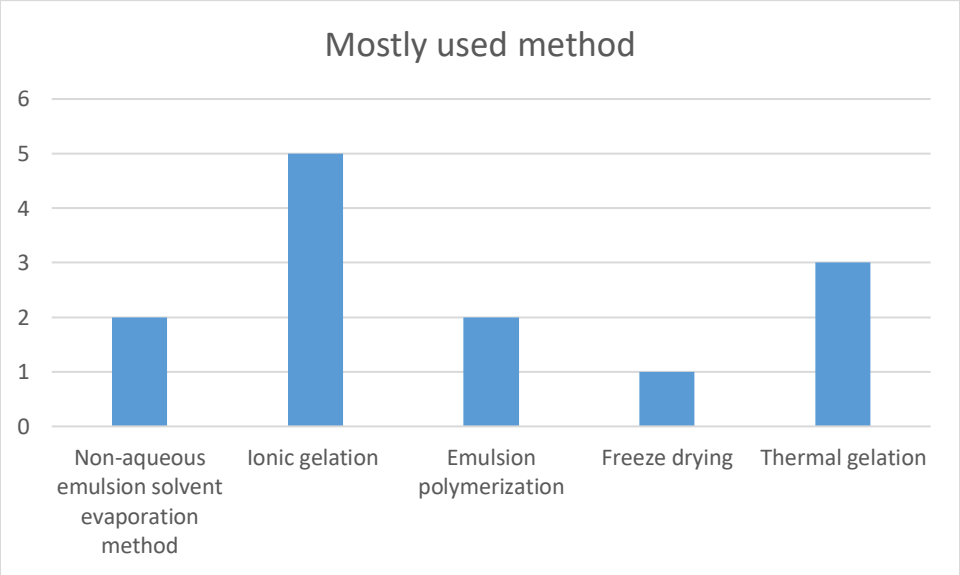

Fig 16: Mostly used method

Discussion: There are several method by which pellets can be formed. According this review mostly used method is ionic gelation. This method is more convenient and easy. [39-58]

5.1.3. Most efficient method

For microencapsulation of a variety of medicines, the methods described above are extensively utilized.

Method	Average efficient
Non-aqueous emulsion solvent evaporation method	79.50%
Ionic gelation	90%
Emulsion polymerization	50.58%

Table 7: Most efficient method

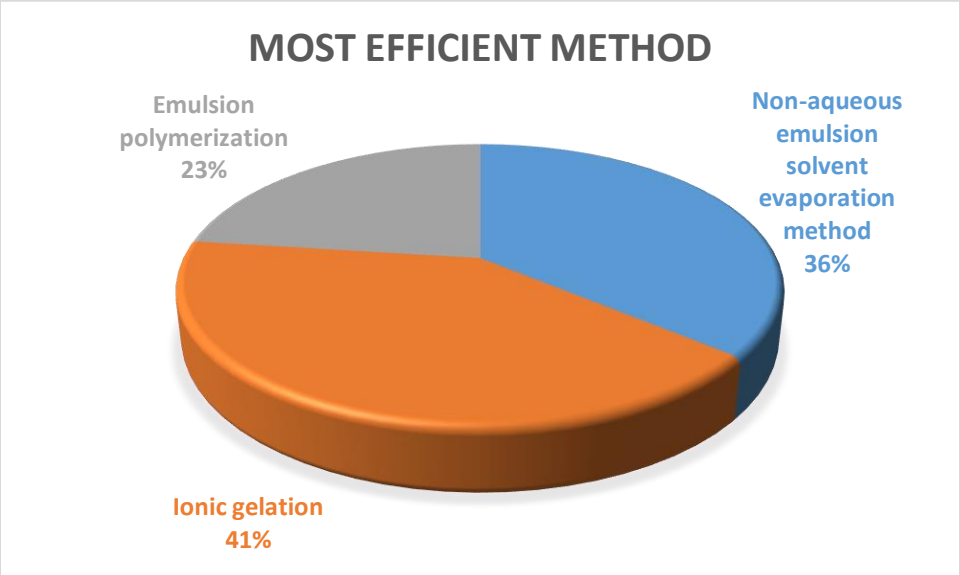

Fig 17: Most efficient method

Discussion: According to this review the most commonly method is ionic gelation (fig 16) and it is the most efficient method. The efficacy of this method is 41%. [39-58]

Development of pellets

5.2.1. Development-1

HPMC is widely utilized as a tablet film coating polymer and is employed as a binder at concentrations of 2%–5% w/w.

Serial No	Concentration of Diclofenac	Concentration of sodium alginate	Concentration of HPMC	Calcium Chloride($Cacl_2$)
T-1	5 mg/ml	2.5%	2%	3%

Table 8: Development of pellets one

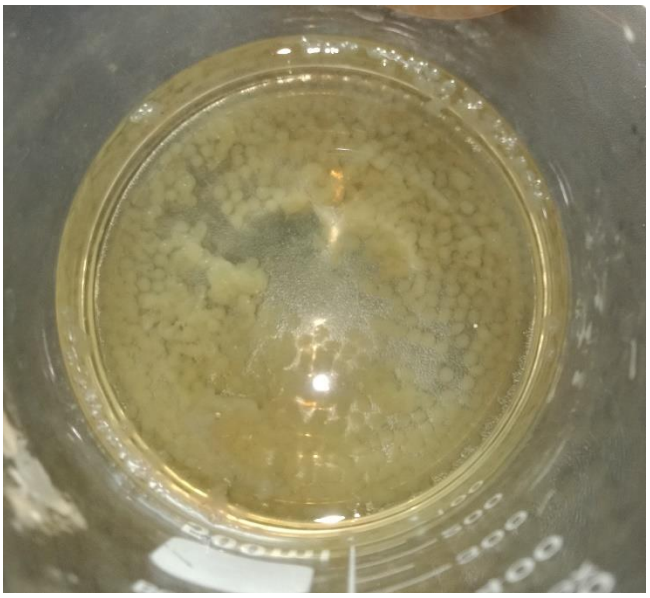

Fig 18: Pellets

Discussion:

Size: undefined

Shape: Some are attached together and some are round shape

Color: Yellowish

Comment: Not acceptable

5.2.2. Development-2

In pharmaceutical formulations, sodium alginate is utilized as a gel. Brown seaweed is used to produce sodium alginate (E401). It serves as a thickener, stabilizer, and emulsifier, among other things.

Serial No	Concentration of Diclofenac	Concentration of sodium alginate	Concentration of HPMC	Calcium Chloride($Cacl_2$)
T-2	5 mg/ml	3%	3%	3%

Table 9: Development of pellets two

Fig 19: pellets

Discussion:

Size: undefined

Shape: Round shape

Color: Yellowish

Comment: each pellets are single and this condition can be acceptable

5.3. Load of rabeprazole

Peptic ulcer disease, gastroesophageal reflux disease, and excessive stomach acid production are all treated with this medication. It releases first and neutralizes acid secretion since it is loaded on the surface of the pellets.

Serial No	Concentration of Rabeprazole
F-1	1 mg/ml

Table 10: Load of rabepazole

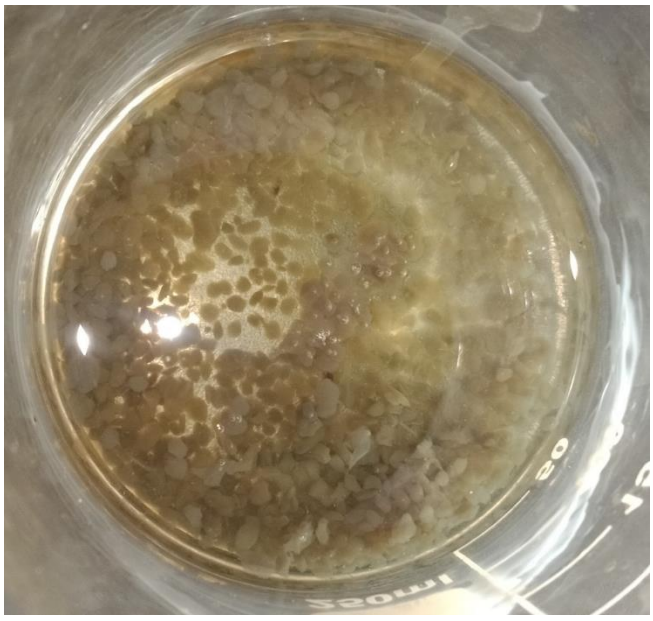

Fig 20: Load of rabeprazole

Discussion:

Size: undefined

Shape: Some are round shape and quadrilateral shape

Color: Brownish

Comment: each pellets are single and this condition can be acceptable

5.4. Physical properties

Without altering the composition of matter, physical characteristics may be seen and quantified. To observe and characterize matter, physical characteristics are used..

Fig 21: Dry pellets

Discussion:

Color: Brown

Odor: odorless

Shape: Some are round shape and quadrilateral shape

Size: undefined

Weight: 460.85 mg

Conclusion

Conclusion

Ionic gelation, using Sodium alginate (3%) and HPMC (3%) as drug release retarding polymers, is a good way to make Diclofenac and Rabeprazole microspheres in combination. The look of the pellets was satisfactory after the Rabeprazole load. Rabeprazole is the first drug introduced in this combination. This pre-determined medicine combination will be beneficial in relieving discomfort without the need for additional antiulcer medication. The frequency of medication administration will be reduced as a result of the prolonged release of medicines, and patient compliance will be improved.

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