WWW.IJRPR.COM

International Journal of Research Publication and Reviews

Journal homepage: www.ijrpr.com ISSN 2582-7421

REVIEW ON MICROENCAPSULATION

SHIRSATH VITTHAL G.*, SHAIKH ARFAT SHAIKH GANI*, MORE SAGAR N.*, DR. SUNIL KOLHE

ACS'S COLLEGE OF PHARMACEUTICAL SCIENCE AND RES, ASHTI, BEED-414203
E-MAIL-SAISHIRSATH05@GMAIL.COM

ABSTRACT :

The controlled release drug delivery system targets a specific place over an extended period of time by releasing the active medication or substance at a predefined rate. Because it allows for an infinite number of core and shell material combinations, microencapsulation offers a promising medication delivery method that targets certain gastrointestinal tract regions. The definition of a microcapsule, the rationale behind microencapsulation, the different kinds of microcapsules, the drug release mechanism, the kinds of coating materials, the methods for making microcapsules, and their uses are all covered in this overview.

Keywords: Microcapsules, Miniature, Shell, Core, Applications

INTRODUCTION :

The process of encapsulating a material inside a tiny capsule is known as microencapsulation. Microcapsules are tiny spheres surrounded by a consistent wall. The wall of the microcapsule is frequently referred to as a shell or coating, while the substance inside is known as the core or internal phase. Microcapsules range in size from 1 μ to 7 mm.The size and shape of capsules can be affected by the encapsulation of all three states—solid, liquid, and gaseous (Leon and Herbert, 1990).

The resulting capsule may have an uneven shape if the core is made of a solid or crystalline substance. Simple spherical capsules with a single encapsulate droplet may form if the core ingredient is liquid.

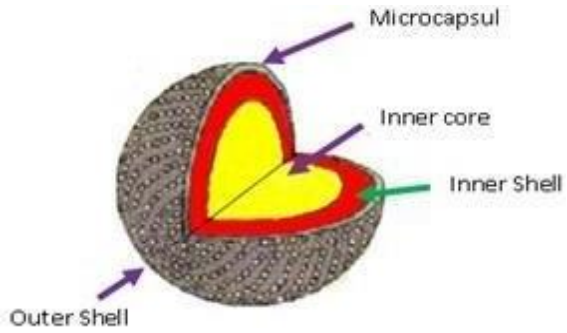
The process of creating thin wall material coatings around substances—which could be solids, liquids, or even gases—encased in microscopic particles is known as microencapsulation. This method was developed in the late 1930s in response to the business machines industry's need for a cleaner alternative to carbon paper and carbon ribbons. The 1950s saw the development of paper and ribbons that contained dyes in microscopic gelatin capsules that were released when a typewriter key or the pressure of a pen or pencil struck them.

By delivering the agent to the target tissue in the optimal amount in the right period of time, maximum therapeutic efficacy, little toxicity and minimal side effects can be achieved. There are various approaches in delivering a therapeutic substance to the target site in a sustained controlled release fashion. One such approach is using microspheres as carriers for drugs.

An appropriate motto for microencapsulation would be 'Small is better'. In its simplest form, a microcapsule is a small sphere with an uniform wall around it. The material inside the microcapsule is known as the core, fill, or internal phase, whereas the wall is called a shell, membrane or coating.

Microspheres are thought of as particles that flow freely and contain biodegradable polymers. Controlling the release characteristics of various coated materials, turning liquids into solids, altering colloidal and surface properties, and protecting the environment are all made possible by the microcapsulation process. Microcapsulation's benefit is the tiny size of the coated
particles, as well as their subsequent application and modification to a broad range of product applications and dosage formats. Due to their tiny size, drug moieties can be broadly dispersed throughout the gastrointestinal tract, which may enhance drug sorption. The microencapsulated items are regarded as being larger than 1 micrometer and having a diameter of up to 1000 micrometers. 10–90% w/w core is present in commercially accessible microparticles. By regulating the drug's rate of release from the dosage form, microencapsulation technology allows form the regulation of the drug's absorption rate.

Figure 1: Structure of microcapsule



Coating materials :

The choice of coating materials affects the final microcapsules' or microspheres' chemical and physical characteristics. These polymers could be hydrophilic, hydrophobic, or a mix of the two. Alginates7, gelatin, polyvinyl alcohol, ethyl cellulose, and cellulose acetate are a few coating materials that have been effectively employed. It need to create a film that blends in with the main substance.

Coating material properties :

- Controlled release under specific conditions.
- Stable towards core material.
- Inert toward active ingredients.
- Stable Film-forming, tasteless,
- Economical.
- The coating can be flexible, hard, thin etc.
- Soluble in an aqueous media or solvent, or melting.

Reasons for Microcapsulation :

There are innumerable justifications for microencapsulation. Certain situations require the core to be separated from its environment, such as protecting vitamins from oxygen's damaging effects, delaying the evaporation of a volatile core, enhancing the handling qualities of a sticky substance, or shielding a reactive core from chemical assault. Materials may be enclosed for a number of reasons.

1. It is mainly used to increase the stability, and sustained/prolonged release of the product.
2. Controlling the release rate of the drug from the microcapsules.
3. This technique was widely used for masking taste and odour of many drugs and to improve patient compliance.
4. For converting liquid drugs into a free flowing powder.
5. To reduce the toxicity and GI irritation and many major side effects of the drugs
6. Alteration in site of absorption can be achieved by microencapsulation (James, 2002; Bansode *et al.*, 2010).
7. To formulate a sustained or prolonged release of the drug.
8. To improve patient compliance by masking the unacceptable taste and odor.
9. To convert the liquid drugs in a free flowing powder.
10. To protect the drug from moisture, light and oxygen, e.g. Nifedipine
11. To prevent the incompatibility between drugs
12. To prevent the volatilization of drugs at room temperature like Aspirin and peppermint oil.
13. To reduce the toxicity and GI irritation produced with KCl and ferrous sulphate.
14. To change the site of absorption.
15. To isolate vitamins from the deteriorating effects of oxygen such as microencapsulated vitamin A palmitate had enhanced stability, as prevent from oxidation.
16. To prepare intrauterine contraceptive device.
17. To protect the immediate environment of the microcapsules from the active components.
18. To reduce the possibility of sensitization of factorial person such as insecticides.

Difficulties in Microencapsulation Technique :

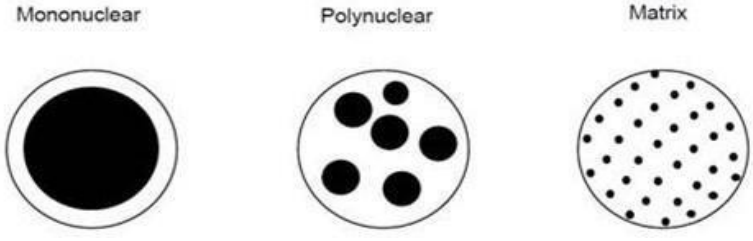
I. Incomplete or discontinuous coating
II. Inadequate stability or shelf life of sensitivepharmaceuticals
III. Non reproducible and unstable release characteristicsof coated products
IV. Economic limitations

Classification :-

Microcapsules can be classified on three basic categories according to their morphology as follows,

1. Mononuclear / single core.
2. Polynuclear/ multiple core.
3. Matrix type (Jyothi, 2012).

Figure 2: Types of microcapsules



Microcapsules can be classified into three basic morphologies: mononuclear (core-shell) microcapsules, which have a shell around the core, polynuclear capsules, which have multiple cores enclosed within the shell, and matrix encapsulation, which has the core material uniformly distributed into the shell material.

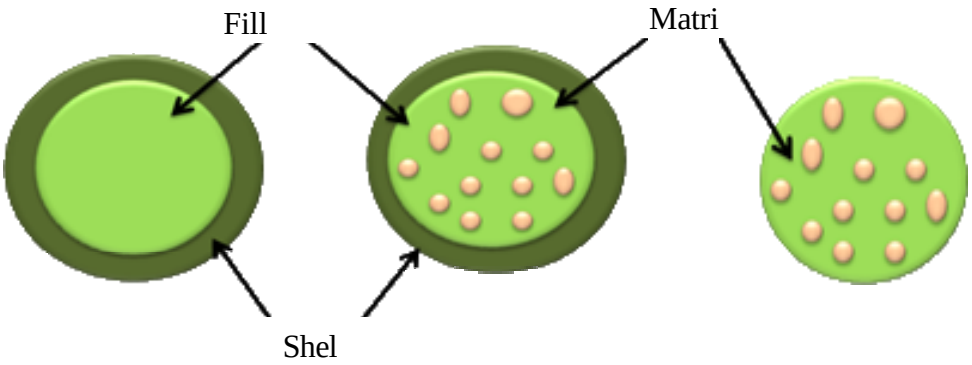


Figure 2: Parts of microcapsules

Mechanism of Drug Release from Microcapsules :-

It involves 4 different mechanisms (Brazel and Peppas, 2000)

1. **Diffusion controlled monolithic system:** It is the most widely used method of medication release from core material, where the dissolving fluid enters the shell, contacts the core, and then leaks through pores or interstitial channels. The release of the medication is dependent on
   - The rate of drug dissolution in dissolution fluid**.**
   - Rate of penetration of dissolution fluid to the microcapsules and rate at which the dissolved drug escapes from the microcapsules.

   The Higuchi equation governs the rate kinetics of medication release. (D/J (2A-€ CS)CSt) = Q½ In time t, Q is the amount of drug release per unit area of exposed surface. J is the capillary system's tortuosity in the wall. D is the solute's diffusion coefficient in solution. A is the total drug content per volume unit. € is the porosity of the microcapsule wall. CS stands for the drug's solubility in the permeating dissolving fluid.
2. **Dissolution:** When a polymer coat is soluble in a dissolving fluid, the rate at which the coat dissolves determines the rate at which the medicine is released. It also depends on the coat material's thickness and solubility in the dissolving solvent. Either the capsule wall melts or the coat dissolves, releasing the medication**.**
3. **Degradation controlled monolithic system:** The medication is dispersed throughout the core after dissolving in the matrix. When the matrix breaks down, the medicine that is affixed to it is released. The drug's diffusion is slower than the matrix's degradation.
4. **Erosion:** The pH or enzymatic hydrolysis of the coat causes the medication to be released by erosion process. Microcapsule medication release has grown more complicated. Microcapsules differ in their size, shape, and the way their core and coat materials are arranged. the physical- chemical characteristics of coating materials, such as thickness and porosity, and core material characteristics, such as solubility, diffusibility, and partition coefficient. Microcapsules release a specific amount of medicine over a predetermined length of time, following zero order kinetics, which means that the release rate is constant. The first half of the total drug release from monolithic microcapsules is t½ dependent, and then it decreases exponentially (Sachan, 2005).

Development of Microcapsules

1. Core materia;The particular substance to be coated, whether it be liquid or solid, is referred to as the core material. While the liquid core contains the dissolved ingredients, the solid core may contain the active substance, stabilizers, diluents, excipients, and release rate retardantsl.

2. Coating material: Coating materials are defined as a layer of substance covered over the core for production of the drug. The coating material should possess properties such as

- It should have controlled release under specific co nditions, soluble in aqueous media/solvent.
- It should possess sufficient properties such as flexibility, strength, impermeability, stability and optical properties.
- It should be chemically compatible with the core and non
- It should be ca pable of forming a film.

-reactive.

Types of coating materials: Depending upon origin (Shekhar et al., 2010).

Table 1: Types Of Coating Materials

POLYMERS	EXAMPLES
1. **1.NATURAL POLYMERS**:	
A.Proteins:	Albumin Gelatin Collagen.
B.Carbohydrates:	Agarose Chitosan Starch Carragenan
C.Chemically modified carbohydrates	polystarch Polydextran
2.SYNTHETIC POLYMERS:	
A.Biodegradable:	Lactides Glycolides and co polymers Poly alkly cyanoacrylates Poly anhydrides
B.Non biodegradable :	poly methyl methacrylate (PMMA) Acrolein Glycidyl methacrylate Epoxy polymers

POLYMERS ..	EXAMPLES
DEPENDING UPON SOLUBILITY: **1.Water soluble resins:**	Gelatin Gum arabic Starch Poly vinyl pylorridine Methyl cellulose Carboxy methyl cellulose Hydroxy ethyl cellulose Poly vinyl alcohol Arabinogalactan Polyacrylic acid.
2.Water insoluble resins :	Ethyl cellulose Poly ethylene Polymethacrylate Polyamide (Nylon) Poly (Ethylene vinyl acetate) Cellulose nitrates Silicones Poly (lactide-co-gylcolide)
3.Waxes and Lipids :	paraffin Carnauba. Spermaceti Bees wax Stearic acid Stearyl alcohol Glyceryl stearate
4.Enteric resins :	Shellac Cellulose acetate phthalate Zein

Factors Influencing Properties of Microcapsules :-

1. Properties of material :

a. Dispersed phase
b. Continuous phase

The polymer plays an important role in encapsulating the drug which depends on

i. The solubility of the polymer.
ii. The concentration of polymer.
iii. The organic solvent used.
iv. Rate of solvent removal.
v. Dispersed and continuous phase ratio.
vi. Nature of the drug –hydrophilic /hydrophobic

The drug's encapsulation efficiency rises with increasing polymer concentration, and the drug's release is sustained if the dispersion phase is extremely viscous because it lowers the microcapsules' porosity. The rate at which microcapsules solidify is influenced by the ratio of dispersed to continuous phases.The microcapsules solidify quickly if the volume of the continuous phase is large because it dilutes the organic solvent and creates a strong concentration gradient across the phase boundary. The microcapsules' particle size is influenced by this rate of solidification; as the volume of continuous phase grows, so does the particle size. Temperature affects the rate of solvent removal; a quick rise in temperature causes a thin wall and a huge hollow core, which causes the drug to burst out, while a gradual rise in temperature causes the core size to decrease, which controls drug release. The cloud point (Cs) of the organic solvent used determines how soluble the polymer is; the higher the Cs, the more soluble the polymer is, and the more organic solvent is needed for it to precipitate out of the polymeric solution.

Parameters to Be Considered for the Formulation :-

- Viscosity of dispersed phase.
- Volume fraction of dispersed phase to continuous phase.
- Quantity of drug in dispersed phase.
- Concentration of surfactant.
- Operating parameters:
- Agitation rate
- Temperature
- Pressure
- Geometry of reactor and agitator.

Techniques for Preparation of Microcapsules :-

1. Physical Methods

A. **Air suspension coating**: This process involves dispersing the solid core material into a supporting air stream, coating the suspended particles with polymers through volatile solvent release, and then leaving a very thin layer or film of polymer on the core. Until necessary criteria, including coating thickness, are reached, the operation is repeated multiple times. The air stream that holds the particles in place also aids in their drying. The temperature of the air stream directly correlates with the rate of drying. According to Jackson et al. (1991), the coating chamber is set up so that particles travel upward into the coating zone, then scatter into moving air and return to the base of the coating chamber, repeating the process until the required thickness is reached.

Process variables to be considered during formulation:

- Concentration of coating material.
- Solubility, Melting point, Surface area, Density, Volatility of core material.
- Temperature of air stream, amount of air stream required to fluidize.

B. **Coacervation process**: In order to prevent the core material from dissolving or reacting in the solvent, it is distributed throughout the coating material solution during this procedure. Coacervation happens when the pH of the dispersion changes, which can be accomplished by adding sulfuric acid, HCL, or organic acids. This reduces the solubility of the dispersed phase (shell material) and causes a precipitate to develop from the solution. The shell cools to solidify and creates a microcapsule, while the shell material continuously coats the core. Formaldehyde and other hardening agents may be applied during the procedure. The suspension was dried using a fluidized bed dryer or spray dryer (Nihant et al., 1995).

Disadvantage : Spray drying is only suitable for heat sensitive drugs.

C. **Pan coating:** It is among the oldest techniques still in use in the pharmaceutical sector. This technique involves applying the coating substance gradually while the particles are tumbling in a pan. The core material receives the solution from the atomized spray, and the coating solvent is removed by passing hot air over it. For pan coating, particles larger than 600 μm are basically efficient (Kasturagi et al., 1995).

D. **Centrifugal extrusion process:** This method works best with liquids or slurries. This procedure uses a revolving extrusion head with concentric nozzles to encapsulate the material. A sheath of solution envelops the central liquid jet. The jet splits into core droplets coated with wall solution as it passes through the air. The molten wall is solidified and the solvent may evaporate from the wall solution while the droplets are fluidized or in flight. The droplets settle as a narrow ring around the spray nozzle because their mean diameter is within ±10%. Thus, capsules can be held in a ring-shaped hardening bath to solidify them once they have formed. This method works well for creating 400–2000 μm particles.

E. **Spray drying and congealing method**: This approach is cost-effective and works well for labile medications due to its shorter dryer contact time. The active ingredient is trapped in the dried particle after dissolving or suspending in the polymer solution. The core and coating substance dispersion processes in both approaches are comparable, however the coating solidification rate varies. Whereas spray congealing solidifies by thermally congealing or adding a non-solvent, spray drying involves the quick evaporation of solvent in which the coating material dissolves. Sorption, extraction, and evaporation are the methods used to remove non- solvents (Re, 1998; Poshadri and Aparna, 2010).

A. **Solvent evaporation method:** This method is widely used for water soluble and water insoluble materials to produce solid and liquid core materials.
Numerous polymers or film-forming agents can be employed. This process involves dissolving the coating material (polymer) in a volatile solvent that is incompatible with the liquid vehicle phase. The coating polymer solution dissolves or disperses the core substance (drug) that will be microencapsulated. To create the right size microcapsule, the core coating material combination or dispersion is agitated and distributed in the liquid production vehicle phase. Either constant stirring or the use of an external heat source evaporates the solvent (Jain, 2002).

B. **Interfacial Polymerisation**: The reactants in this process combine at the interphase and undergo a quick reaction. An acid chloride and a substance with an active hydrogen atom, such as an amine, alcohol, polyester, or polyuria, are involved in the reaction. Thin, flexible walls
quickly form at the interface as a result, and the base created during the reaction neutralizes the acid that forms.

C. **Interfacial cross linking:** This process substitutes a polymer, like protein, for the monomer that contains active hydrogen. Consequently, a reaction takes place at the emulsion's interface where the acid chloride combines with different protein functional groups to produce a membrane. This technique was created to prevent the use of harmful diamines.

D. **Insitu polymerisation**: This method involves direct polymerization of a single monomer is carried out on the particle surface. The coating thickness ranges from 0.2-75μm. **E. Matrix polymerisation**: When particles are formed using this process, a core substance is embedded in a polymeric matrix. This process is comparable to spray drying, when the solvent evaporates from the matrix material to generate particles.

Physico-chemical Methods :-

A. **Coacervation phase separation:** It includes 3 stepshttps://en.wikipedia.org/wiki/Micro- encapsulation.

I. Formation of 3 immiscible phases (core material, coating material phase, liquid phase)

II. Deposition of polymer on core material.

III. Rigidisation of coating material.

B. Ionotropic gelation method: This method is based on the ability of polyelectrolytes to crosslink in the presence of counter ions to form

Core material is dispersed in solution of coating polymer, solvent for polymer is vehicle.

↓

Deposition of polymeric solution onto core material.

↓

Deposition of liquid polymer occur when polymer is absorbed at interface between core material and liquid vehicle phase

↓

Rigidisation

↓

Microcapsule

hydrogels. Ionotropic gelation is produced when units of uric acid of the chains in the polymer alginate, crosslink with multivalent cations. These may include calcium, zinc, iron and aluminum. **Applications (Benita, 1996)**

C.

D. □ Microencapsulation has been used to protect drugs from environmental hazards such as

E. humidity, light, oxygen or heat.

A great degree of protection can be provided by microencapsulation. For ex: Vitamin A, K has been shown to be protected from moisture and oxygen.

□ In the field of agriculture microencapsulation has been used to decrease potential danger of handling toxic/noxious substances. Toxicity occurred due to handling of fumigants, herbicides, insectides and pesticides which has been decreased by the use of microencapsulation techniques.

□ To reduce gastric irritation.

In Vaccine Delivery; Because they stabilize and regulate the release of antigens, microcapsules have been employed as carriers.The medication increases patient convenience by reducing the need for several doses. For instance, the lyophilized polymer derived from lactic acid is present in the LUCRIN depot. Leuprolide acetate, an analog of gonadotropin-releasing hormone, is found in the core and is used to treat endometriosis, breast cancer, and prostate cancer (Thies and Bissey, 1983).Potential uses for novel drug delivery systems include regulated and sustained drug delivery. Microencapsulation has shown promise in gene therapy, AIDS, diabetes, malignancies, and the substitution of medicinal drugs.

Application of Microencapsulation :-

Medical Application

1. Release of proteins, hormones and peptides over extended period of time.
2. Gene therapy with DNA plasmids and also delivery of insulin.
3. Vaccine delivery for treatment of diseases like hepatitis, influenza, pertusis, ricin toxoid

NEED OF STUDY :

1. Protection and improved delivery :

Many components, like the essential oils, having numerous benefits like antimicrobial and antioxidant properties, the microorganisms which are used in fermentation and the probiotics, can widely be used in the preparation of functional foods.

2. Controlled release :

Encapsulated functional components like certain vitamins, flavors, or essential oils when incorporated in the food matrix are of importance only when they are released at a particular location in the body or at a particular time, for example, encapsulated flavors in chewing gum are released only when the gum is chewed.

3. Masking of flavor and odor :

Microencapsulation is used for masking the undesirable flavor and aroma of certain compounds before incorporating them into any food. For instance, fish oil and certain bitter tasting compounds can all be used in foods without rendering the food with unpleasant taste and smell

CONCLUSION :

Since the introduction of the controlled drug delivery system concept in the 1970s, microencapsulation has advanced significantly and shown encouraging outcomes. Three phases of matter—solids, liquids, and gases—can be enclosed in this procedure. It turns the liquid medications into a powder that flows freely. It lessens side effects, GI discomfort, and toxicity. By maintaining the drug's release and directing it to the precise location, microcapsules have been shown to be an improved delivery method, which lowers the toxicity.

SUMMERY :

I. an effective protection of the encapsulated active agent against (e.g. enzymatic) degradation
II. the possibility to accurately control the release rate of the incorporated drug over periods of hours to months,
III. an easy administration (compared to alternative parenteral controlled release dosage forms, such as macro-sized implants), and
IV. It is possible to deliver desired, pre-programmed drug release profiles that correspond to the patient's therapeutic requirements. An overview of the general features and most current developments in drug-loaded microparticles to increase the effectiveness of different medical treatments is provided in this article. Controlling the rate of medication delivery to the target site and directing the drug to a particular organ or tissue are two issues that can be resolved with the help of a well-designed controlled release drug delivery system. Formulation scientists have faced difficulties in developing oral controlled release systems since they are unable to confine and localize the system at certain gastrointestinal tract locations. When creating an oral controlled release system, microparticulate drug delivery systems are an intriguing and promising alternative. The objective of this paper is to take a closer look at microparticles as drug delivery devices for increasing efficiency of drug delivery, improving the release profile and drug targeting. In order to appreciate the application possibilities of microcapsules in drug delivery, some fundamental aspects are briefly reviewed.

REFERENCES :

1. Nitika Agnihotri (2012). Microencapsulation – A Novel Approach in Drug Delivery: A Review, Indo Global Journal of Pharmaceutical Sciences, 2012; 2(1): 1-20
2. Krishna Sailaja A (2015). A REVIEW ON MICROCAPSULES, CIBTech Journal of Pharmaceutical Sciences ISSN: 2319–3891 (Online) An Open Access, Online International Journal Available at http://www.cibtech.org/cjps.htm 2015 Vol.4 (2) April-June, pp.26-33/Sailaja and Jyothika
3. Mali Snehal D. (2013) Microencapsulation: A Review, Research J. Pharm. and Tech. 6(9): September 2013
4. Benita Simon (1996). Microencapsulation Methods and Industrial Application, 2nd edition (New York: Taylor & Francis).
5. Jackson LS and Lee K (1991). Microencapsulation and the food industry (htm), Lebennsmittel- Wissenschaft Techonologie. Retrieved on 1991-02-02.
6. Jain NK (2002). Controlled and Novel Drug Delivery, 4th edition (New Delhi, India: CBS Publisher and Distributor) 236-237.
7. James S (2002). Encylopedia of Pharmaceutical Technology, 3rd edition 1325-1333.
8. Jyothi Sri S (2012). Microencapsulation: A Review. International Journal of Pharma and Bio Sciences 3(1) 509-531.
9. Kasturagi Y, Sugiura YC, Lee K, Otsugi and Kurihara (1995). Selective Inhibition of Bitter Taste of Various Drugs By Lipoprotein. Pharmaceutical Research 12(5) 658-662.
10. Leon L, Herbert AL and Joseph LK (1990). The Theory and Practice of Industrial Pharmacy, 3rd edition (Varghese Publishing House) 412, 428
11. Poshadri A and Aparna Kuna (2010). Microencapsulation Technology: A Review. Journal of Research Angrau 38(1) 86-102.
12. Re MI (1998). Microencapsulation by spray drying. Drying Technology 16 1195–1236.
13. Mali Snehal D. (2013) Microencapsulation: A Review, Research J. Pharm. and Tech. 6(9): September 2013