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Microencapsulation of celecoxib using various methods and polymers

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Abstract--Microencapsulation is a process in which active substances are coated by extremely small capsules. It is a new technology that has been used in the cosmetics industry as well as in the pharmaceutical, agrochemical and food industries, being used in flavours, acids, oils, vitamins, microorganisms, among others. This paper provides an UpToDate review of different microencapsulation methods and polymers used specifically for Celecoxib drug. As Celecoxib is poorly soluble in water, there are several methods used to improve solubility and bioavailability using various polymers. The different microencapsulation methods along with different polymers were studied and given a comprehensive review. There are several NSAIDs which are used for pain management and Celecoxib is a non-steroidal anti-inflammatory drug used in the treatment of osteoarthritis, rheumatoid arthritis, acute pain, painful menstruation, and menstrual symptoms. There are many techniques available that can be used to fabricate microcapsules based on desired characteristics, and applications of the final microcapsule formulation. For Celecoxib microencapsulation, Spray drying techniques are widely used method for the research studies. some of the advantages of spray-drying include its ability to be fully

automated and continuous. Other advantages are short residence times and suitability for both heat-sensitive and heat-resistant sample. General parameters used for spray drying of Celecoxib are; Drying gas inlet temperature: 43 to 105°C, Dryer outlet temperature: 30 to 70°C, Solution Flow rate: 5 to 6 ml/min, Drying gas / air flow rate: 35 to 50 m³/hr, Atomization air pressure or Nozzle pressure: 1 to 2kg/cm². Polymers are used widely in pharmaceutical systems as coating materials and, a component of controlled, site at specific drug delivery systems, reduction of toxicity, increase therapeutic efficiency. Some of the general advantages or uses of microencapsulation's are, to mask the core taste, to reduce reactivity of core (bioactive) in relation to outside environment, to increase bioavailability and to alter drug release and has many other uses as well. The coating material or the polymers should be capable of forming a film that is cohesive with the core material and there are many other parameters need to be considered for selection of coating materials, Water soluble polymers like Polyvinylpyrrolidone are widely used for microencapsulation Celecoxib drug.

Keywords---microencapsulation, celecoxib, spray drying, pan coating, fluid bed coating, solvent evaporation, PVP, polymers, non-steroidal anti-inflammatory drug.

Introduction

Microencapsulation is a process in which active substances are coated by extremely small capsules. It is a new technology that has been used in the cosmetics industry as well as in the pharmaceutical, agrochemical and food industries, being used in flavours, acids, oils, vitamins, microorganisms, among others. Some of the general advantages or uses of microencapsulation's are, to mask the core taste, to reduce reactivity of core (bioactive) in relation to outside environment, to increase bioavailability and to alter drug release and has many other uses as well. (Figure-1)

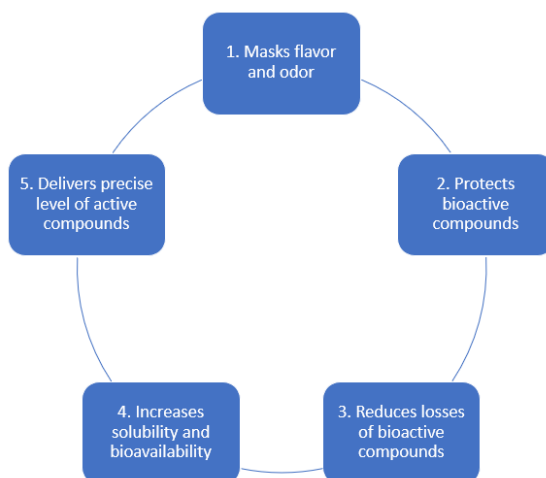


Figure 1. General uses of Microencapsulation

NSAIDs (Non-Steroidal Anti-inflammatory Drugs) reduce pain significantly in patients with arthritis, low back pain and soft tissue pain. NSAIDs reduce pain and inflammatory by blocking cyclo oxygenases (COX), enzymes that are needed to produce prostaglandins. There are several NSAIDs which are used for pain management and Celecoxib is a non-steroidal anti-inflammatory drug used in the treatment of osteoarthritis, rheumatoid arthritis, acute pain, painful menstruation, and menstrual symptoms. The mechanism of action of Celecoxib is due to inhibition of prostaglandin synthesis. And unlike most NSAIDs which inhibit both types of cyclooxygenases (COX-1 and COX-2).⁽¹⁾ This paper provides an UpToDate review of different microencapsulation methods and polymers used specifically for Celecoxib drug. As Celecoxib is poorly soluble in water, there are several methods used to improve solubility and bioavailability was done using many polymers. The different microencapsulation methods of Celecoxib along with various polymers were studied and given a comprehensive review. The first part of the paper represents types of microencapsulation methods used for Celecoxib and second part represent polymers used for microencapsulation of Celecoxib. Table-1 represents the list of Microencapsulation methods, Polymers used for the preparation of Celecoxib microencapsulation.

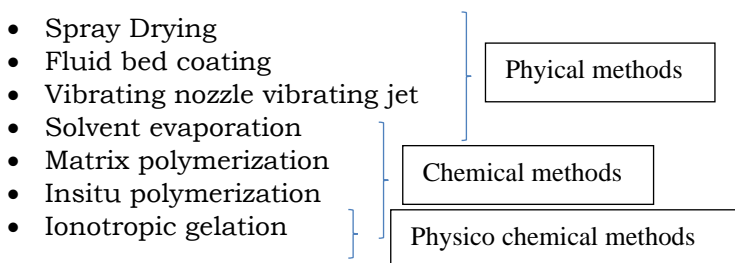
Table 1
List of Polymers and encapsulation methods used for Microencapsulation of Celecoxib

Microencapsulation type/method	Polymers used	Other ingredients used	Size of particle	Reference
Spray drying	PVPK 30, Hydroxy propyl beta cyclodextrin	Methanol	200 to 2000nm	Pawar et al., IJPSR, 2017; Vol. 8(5)
Electro spraying	Poly (lactic-co-glycolic acid) (PLGA)	Acetone, Acetonitrile and Methanol	2 to 7 micrometre diameters	A. Bohr et al. / Polymer 53 (2012)
Spray drying	Hydroxy propyl	Acetone	NA	J. Chen et al.,

	methylcellulose acetate succinate			molecular pharmaceuticals, (2015)
Spray drying	Dextrin	Ethanol	0.5 to 10 micrometres	Cho et al./ American Scientific Publishers, Vol 18, (2018)
Spray drying	Kollicoat IR (MW: 45,000Da), PVA (MW;22,000 & PEG 6000,	Ethanol, water, Dichloromethane	NA	E.A. Fouad et al. Drug Development and Industrial Pharmacy, vol 37, (2011)
Spray drying	Pluronic F 127	Dichloromethane	NA	Mudit Dixit et al, Indian Journal of Pharmaceutical Education and Research,
Spray drying/solvent evaporation/melting methods	Soluplus	Methanol	2.8 to 46 μ m	Homayouni A et al. / IJPR (2015), 14 (1): 35-50
Spray drying	Chitosan		1.8 to 2.7 μ m	Lopedota et al, Pharm Res (2016)
Spray drying	Isomalt, PVP	Ethanol	20 μ m	S. Motallae et al., Journal of Drug Delivery Science and Technology, vol 46 (2018)
Solvent Evaporation	Eudragit L-100, PVP (Polyvinyl pyrrolidone).	Acetone, Liquid paraffin, Tween 80, n-hexane	10.7 to 31.2 μ m	Shahzad et al, Tropical Journal of Pharmaceutical Research (2012); 11 (5): 695-702
Solvent Evaporation	poly- ϵ -caprolactone (PCL), Eudragit® S100	Acetone, Liquid paraffin, Tween 80, n-hexane	60 to 277 μ m	Dalia M. Ghorab et al., Drug Delivery, 2011; 18(7): 523–535
Solvent Evaporation	Polymethacrylate (PMA) and Poly-Vinyl Pyrrolidone-K30 (PVP)	Acetone, Liquid paraffin, Tween 80, n-hexane	NA	Muhammad Khurram Shahzad et al., J.Chem.Soc. Pak., Vol. 34, No. 3, 2012 741

Various Microencapsulation methods used for Celecoxib

There are many techniques available that can be used to fabricate microcapsules based on desired characteristics, and applications of the final microcapsule formulation.^{R-2} For Microencapsulation of Celecoxib requires consideration of polymers and Drug material properties like solubility, miscibility, coating properties etc. Below listed are some of the microencapsulation techniques widely used for microencapsulation of Celecoxib and this list is based on the vast literature search. These are broadly classified as physical, chemical, and physico chemical method as listed below,



For each of these microencapsulation method of Celecoxib, suitable examples were discussed below with respect to preparation of microencapsulated particles using various polymers with Celecoxib drug molecule.

Spray drying

Spray drying is one of the most widely used microencapsulation techniques since it provides rapid evaporation of water and maintains the low temperature in the particles. Prior to spray drying, the wall material is mixed with the suspension containing encapsulated components through intensive homogenization.^{R-3}. Research by Pawar et al., Preparation of spray dried amorphous ternary system (ATS): The spray drying operation was performed using a spray dryer (Labultima LU-222). Appropriate weights of CLX, PVP K30 and Hydroxy Propyl β Cyclodextrin (HPB) as per DoE in all runs were added to 99.8% methanol. The spray drying was performed with the following conditions: inlet temperature of 90°C and outlet temperature 70°C, solution flow rate 5 ml/min at speed 5 ml/min and aspirator 65%; feed rate 12%; atomization air pressure 1.75 Kg/cm². The spray dried particles were stored in a desiccator until used for further studies. These results demonstrated the effectiveness of the proposed jointed use of PVP K30 and HPB, as well as the usefulness of the multivariate approach for the preparation of ATS. Validated optimum ATS were characterized by DSC, XRD, SEM and particle size analysis. Characterization results confirmed the formation of amorphous ternary system with average particle size 727.9 \pm 260.6nm.^{R-4}

Research by Chen Jie et al., Solid dispersions of celecoxib in HPMCAS at a drug loading of 33.3 w/w% (COX/HPMCAS DL 33.3 w/w%) were prepared by spray drying. Celecoxib and HPMCAS were dissolved in acetone at 20 mg/mL and 40 mg/mL, respectively. The mixture was alternately stirred on a magnetic stir plate and submersed into a Branson Ultra-Sonicator until all components had dissolved. Materials were spray dried using a ProCepT Microspray Dryer with a bifluid nozzle. Key operation parameters include nozzle size (0.8 mm), spray rate

(6 mL/min), inlet temperature (85 +/- 5°C), outlet drying temperature (55 +/- 5°C) and atomization air flow (4 L/min). The spray dried dispersion was collected using small cyclone separation. Solids were stored in a vacuum oven overnight at room temperature for secondary drying. Apart from usage of polymers, the impact of surfactant was also studied in this paper and concluded that surfactant choice is critical to avoid failure of amorphous solid dispersions through crystallization of the drug. ^{R-5}

Research by Cho et al. Dextrin (18.8 g) and celecoxib (1 g) were dissolved in ethanol (105 mL) and distilled water (45 mL), respectively. Then, the dextrin solution was slowly poured into ethanol solution under mechanical mixing. The mixture was pre-warmed at 40–50°C and blended with 0.2 g SLS to form a free-flowing particles. The resulting mixture was spray-dried by an Eyela SD-1000 spray dryer system (Tokyo, Japan) equipped under the following operational conditions: in-let air temperature, 60, 90, 120, 150°C; pump speed, 3–5 mL/min; air blowing level, 0.5; atomizing level, 10. Prepared samples were harvested from product vessel and immediately stored (under refrigeration condition, 4±1.0°C) in tightly sealed containers. The dissolution profile of celecoxib from DE proved to be much higher than that of celecoxib powder due to the nano-structured matrix, amorphous state, and encapsulated ethanol. ^{R-6}

Research by E.A. Fouad et al. Celecoxib in combination with PEG 6000 in different mass ratios (1:1, 1:2, and 1:4) was dissolved in 100 mL of dichloromethane. To these clear solutions, silicon dioxide (2% w/v) was slowly added to obtain uniform suspensions. The suspension was spray-dried in the Büchi mini spray-dryer with the following conditions: inlet temperature 50°C, outlet temperature 30°C, solution flow rate 5 mL/min, air flow rate 40–50 m³ /h, and atomizing air pressure 1.0–1.1 bar. The batch size was again 10 g. The present research investigates the enhancement of the dissolution rate of celecoxib by using spray-drying to prepare a solid dispersion with various polymers, namely Kollicoat IR® (Kollicoat), polyvinyl alcohol (PVA) 22000, or polyethylene glycol 6000 (PEG). The investigated drug-to-polymer mass ratios were 1:1, 1:2, and 1:4 by weight. Hydroalcoholic or methylene chloride solvent systems were used. The obtained yields ranged from 65% to 78%, whereas the entrapment efficiencies were between 68% and 82%. The results revealed an increase in the dissolution rate of the prepared particles up to 200% within 20min. The prepared particles were investigated using differential scanning calorimetry, scanning electron microscopy, X-ray diffraction, and Fourier transform infrared spectroscopy. The increased dissolution rate was attributed to hydrogen bond formation between celecoxib and each polymer together with the reduced size of the formed particles offering a greater overall surface area. It was concluded that spray-drying may be considered a successful one-step technique to improve the dissolution rate of celecoxib when using Kollicoat, PVA, or PEG as the carrier polymer. ^{R-7}

Research by Mudit Dixit et al. The microspheres were prepared by spray-drying technique. The spray drying was performed by Mini Spray Dryer LSD - 48; (Jay instrument & systems Pvt. Ltd. Mumbai). The different drug–polymer ratios used for various microsphere formulations were prepared. The polymer solution was prepared by adding given quantity of polymer to the dichloromethane as solvent. The given quantity of celecoxib was added to the polymer solution and the

resulting mixture was spray dried. Following are the spray drier parameters used, Inlet temperature (43°C), Feed pump speed 15%, Vacuum -70(mm Wc), Aspirator level 2 (kg/cm).^{R-8}

Research by Homayouni A et al. In this method, dispersions were prepared by spray drying of methanolic solutions of Celecoxib and SOLUPLUS in specified mass ratios with an overall concentration of 5% (w/v) in a Büchi Mini Spray Dryer B290, Inert Loop B-295 (Büchi Labortechnik AG, Flawil, Switzerland). The spray drying was performed with the following conditions: inlet temperature 80 °C, outlet temperature 50 °C, solution flow rate 5 mL/ min and N₂ flow rate 35 m³ /h. The spray dried samples were stored in a desiccator until used for further studies. It was concluded that SOLUPLUS was a proper carrier to enhance the dissolution rate of Celecoxib. At high SOLUPLUS ratios the method of preparation of dispersed samples had no effect on dissolution rate, whilst at low SOLUPLUS content spray drying was more efficient method.^{R-9}

Research by S Motallae et al. Preparation of CLX:ISO:PVP solid dispersions via spray drying (SD) Accurate amounts of different ratios of CLX and ISO (7:3, 5:5, 3:7, 1:9) and CLX, ISO and PVP (3:5:2, 3:2:5) were weighed. The aforementioned ratios of celecoxib and isomalt were dispersed in a specific amount of 96% ethanol since celecoxib is soluble in ethanol. However, isomalt is insoluble in ethanol, so a specific type of isomalt (Galen IQ 810) with a small particle size (mean particle size: 22 µm) was used in order to prevent blocking of the spray dryer nozzle. The spray drying operation was performed using a B290 mini spray dryer with a B-295 inert loop (Büchi Labortechnik AG, Flawil, Switzerland). Appropriate mass ratios were prepared from 2% w/v ethanolic suspensions. The spray drying was performed with the following conditions: inlet temperature 105°C, outlet temperature 60°C, suspension flow rate of about 5 mL/min, and N₂ atomized flow rate of 35 m³/h. The spray-dried particles were stored in closed vials until needed for further studies. The CLX:PVP:ISO 3:5:2 spray dried sample showed the highest dissolution rate in both media. Exposure of samples to high moisture (75% humidity) recrystallized some of the amorphous CLX. Thus, the results showed that the dissolution rate of CLX was enhanced in 0.25% SLS, whereas a reduction in dissolution rate was observed in 0.04 M Na₃PO₄.^{R-10}

Fluid bed coating

Fluid bed coating is a microencapsulation technique used extensively to encapsulate pharmaceuticals into coated particles or tablets. It is one of the oldest industrial procedures where solid particles are mixed with a dry coating material that is heated to surround the particles cores. Solid particles (or liquid absorbed into porous solids) are suspended on a jet of air followed by the application of a coating material using a liquid spray. The resulting shell is solidified by cooling or solvent vaporization, and the process is repeated until the microcapsule walls are of the desired thickness.

Research by Jin kwon et al, Solid dispersion granules (SDGs) were prepared using a top-spray technique in an Enger fluid-bed granulator (Chongqing, China). Cre-RH (1, 2, and 5 g) were dissolved in 250 mL of an aqueous solution (with 2.5 g HPMC) at 50 °C. Then, 10 g of CXB powder was slowly added to the solution and

stirred for several hours to obtain a homogenous state. The resulting homogeneous solution was sprayed under appropriate conditions on a flowing mixture (microcrystalline cellulose 60 g, lactose 30 g, crospovidone 3 g, Aerosil 200 1.5 g, and talc 3 g) in a fluid-bed granulator. Three types of granules (SDG (CXB/Cre-RH = 1:0.1), SDG (CXB/Cre-RH = 1:0.25), SDG (CXB/Cre-RH = 1:0.5)) were prepared according to the amount of Cre-RH. The process parameters of the granulation were as follows: inlet air temperature, 70–80 °C; product temperature, 25–35 °C; and atomization pressure, 2.0–3.0 bar. After the formation of granules in a fluid-bed granulator, an additional drying process was carried out for 20 min at an inlet air temperature of 50 °C. Magnesium stearate (1%, w/w) was added to the obtained SDGs for lubrication efficacy, and the powder containing the SDGs was passed through a sieve to remove coarse particles. The obtained mixture was mixed in a V-type mixer for 5 min at 30 rpm and then compressed into tablets (equivalent to 50 mg CXB) at a compression level of 7.0–8.0 (about 1000–1500 Kg/cm²) using a single-type Riva SA Minipress MII tableting machine (Buenos Aires, Argentina) equipped with 11.0 mm round punches.^{R-11}

Vibrating nozzle vibrating jet

Vibrating nozzle also termed Vibrating jet is a popular microencapsulation method. The liquid material to be encapsulated is extruded through a nozzle at a specific flow rate, forming a laminar jet. This method uses a permanent sinusoidal force at determined frequencies, forming a microcapsule of uniform distribution. Research by A. Zvonar et al, NP were prepared by modifying the nanoprecipitation technique, as previously applied to the preparation of NP (Fessi et al. 1989). The modification was based on the use of the vibrating nozzle device (Encapsulator Table 1. PLA/PGA ratio and molecular weight of different polymers. Type of polymer PLA/PGA ratio Mw [Da] Terminal carboxyl groups RG 502 50/50 14 000 Esterified RG 752 75/25 20 000 Esterified R 202 H 100/0 17 000 Unesterified High celecoxib-loaded nanoparticles prepared by a vibrating nozzle device 749 Journal of Microencapsulation Downloaded from informahealthcare.com by University of Connecticut on 05/01/13 For personal use only. Inotech IE-50 R, Inotech, Switzerland), originally used for forming pellets and microcapsules; 550 mg of PLA or PLGA and various amounts of celecoxib (27.5, 55 and 110 mg) were dissolved in 15 mL of acetone and the dispersion was pumped through a 500 mm nozzle of an encapsulator at a flow rate of 9 mL min⁻¹ and allowed to drop into 200 mL of aqueous polyvinyl alcohol solution (0.1–0.9% w/w), which was stirred magnetically. The vibration frequency used to break up the liquid jet was set at 482 Hz and the amplitude at 3.5. The voltage applied to charge the surface of the droplets was 930 V. The organic solvent was evaporated for at least 12 h at room temperature with magnetic stirring. The NP dispersion was then filtered through a coarse filter to remove any large aggregates. Drug-free NP were prepared according to the same procedure, but without celecoxib.^{R-12}

Solvent evaporation

Solvent evaporation technique is chemical method of microencapsulation. Solvent evaporation is a technique used by many companies to produce microcapsules specifically for drug encapsulation as the method often requires heat. The process involves that the core material be dissolved / dispersed in the coating solution

followed by agitation in the liquid vehicle to obtain the desired microcapsule size. This mixture is then heated to evaporate the solvent followed by temperature reduction. Research by Shahzad et al; Microspheres were prepared by solvent evaporation technique. Different ratios of Eudragit L-100/polyvinyl pyrrolidone (PVP) were dissolved in 40 ml acetone using a magnetic stirrer. Celecoxib was dispersed in the polymer solution and stirred for 15 min. The resulting dispersion was mechanically added in a thin stream to a mixture of 360 ml light liquid paraffin, 0.5% Tween-80 and 40 ml n-hexane contained in a 500 ml beaker. Stirring at 700 rpm was continued for 3 h, until the acetone evaporated completely. The microspheres formed were collected by filtration on Whatman filter paper no.1 and washed 4 - 5 times with n-hexane. The product was then air-dried at room temperature for 12 h. Formulations were coded as F1, F2, F3, F4, F5, F6, F7, F8, F9, F10, F11, F12 and F13, respectively, as per Table 1. All the batches were prepared in triplicate (n = 3). The experiments were performed in random order. ^{R-13}

Research by Muhammad Khurram Shahzad et al., Microspheres were prepared by solvent evaporation technique. Different ratios of Celecoxib, PMA and PVP were dissolved in 40 ml of acetone using a magnetic stirrer. Then the core material, Celecoxib, was added to the polymers solution and stirred for further 15 minutes. The resulting dispersion was added slowly to a mixture of 360 ml light liquid paraffin, 0.5% tween 80 and 40 ml n-hexane contained in a 500 ml beaker. A mechanical stirrer, with a blade of 4 cm diameter, was used to stir the solution at 700 rpm for 3 hrs until acetone was evaporated completely. The microspheres formed were collected by filtration on Whatman filter paper #1 and were washed for 5 times with n-hexane ^{R-14}

Research by Miha et al. Celecoxib loaded microparticles were prepared using an emulsion method followed by solvent evaporation. Polymers and celecoxib were mixed in a ratio 10:1 and 220 mg of the mixture was dissolved in 2 ml of methylene chloride. In the case of ethyl cellulose 100, four ml of methylene chloride were used to ensure suitable viscosity. Due to the low solubility in methylene chloride, cellulose acetate was dissolved in 6 ml of a mixture of methylene chloride and Isopropanol (7:3). Polymer solutions were added to 20 ml of 0.1% (m/m) aqueous PVA solution and mixed for 2 minutes at 8000 rpm with Ultraturrax T25 (Ika, Germany). The resulting O/W emulsion was mixed for 50 minutes with a propeller stirrer at 2000 rpm (Ika, Germany) in order to allow solvent evaporation. The resulting microparticles were collected by filtration through 0.45 µm HA filter (Millipore, USA) using a vacuum pump and dried at room temperature for 24 hours or 4 days in the case of cellulose acetate. ^{R-15}

Ionotropic gelation

Ionotropic gelation is a physicochemical method of microencapsulation. Ionotropic gelation relies on the ability of polyelectrolytes to cross link when in the presence of counter ions leading to the gelation. This process has been extensively studied using natural polyelectrolytes such as alginate, chitosan, Carboxymethylcellulose, and gellan gum. Gelated beads are produced by the addition of polymeric drops, containing the anionic therapeutic to be encapsulated into an aqueous solution of polyvalent cations. Ionic cross-linking forms a three-dimensional lattice due to the

diffusion of cations into the polymeric drops. Research by Lorena Segale et al, Preparation of Calcium Alginate Beads. Calcium alginate beads were prepared by gelation method using calcium ions as cross-linking agent. In detail, a 1.5% (w/w) sodium alginate aqueous solution was mixed with a drug loaded self-emulsifying phase in 4: 1 ratio and added drop by drop to a 100 mM CaCl₂ solution. The self-emulsifying phase was prepared mixing weighed amounts of Labrasol and TPGS at 50°C and dissolving celecoxib in the excipient solution. The emulsion (sodium alginate solution and self-emulsifying phase) was manually extruded in the hardening bath through needles with 400 or 600 μm inner diameter, under constant gentle stirring, at room temperature. After 15 minutes, the beads were collected, washed with deionised water to eliminate the excess of calcium ions, and then dried at 40°C overnight. The composition of prepared formulations, coded CAI 600 and CAI 400, was listed, Preparation of Calcium Alginate-Chitosan Beads. Calcium alginate-chitosan beads (identified as CAICh 600 and CAICh 400) were prepared according to the one step method. The procedure was identical to that adopted in the case of alginate beads with the exception that the hardening bath was a 0.2% (w/w) chitosan solution in diluted acetic acid (1%) containing CaCl₂ at a concentration of 100 mM. The composition of the chitosan formulations was reported.

Various Polymers used for Microencapsulation of Celecoxib

There are several polymers used for the microencapsulation techniques. Polymers are substances of high molecular weight made up by repeating monomer units. Polymer molecules may be linear, or branched, and separate linear or branched chains may be joined by crosslinks. Polymers are used widely in pharmaceutical systems as coating materials, a component of controlled site at specific drug delivery systems, as reduction of toxicity and to increase therapeutic efficiency. These polymers are broadly classified as Synthetic and Natural Polymers. Some of the synthetic polymers are Polymethylmethacrylate (PMMA), Acrolein, Glycidyl methacrylate, Epoxy polymers, Lactides & Glycosides & their copolymers, Polyalkyl cyano acrylates, Polyanhydrides, Polyvinyl pyrrolidone, Cellulose etc. Some of the Natural Polymers are Proteins, Carbohydrates, chemically modified carbohydrates etc.

Apart from polymer, solvents need to be used for microencapsulation, based on the solubility of Celecoxib drug & the specific polymers used, the solvents would be used for the formulation, viz, methanol, Ethanol, Acetone, Acetonitrile, Dichloromethane etc. The coating material should be capable of forming a film that is cohesive with the core material; be chemically compatible and nonreactive with the core material; and provide the desired coating properties, such as strength, flexibility, impermeability, optical properties, and stability. The coating materials used in microencapsulation methods are amenable, to some extent, to in situ modification. The selection of a given coating often can be aided by the review of existing literature.^{R-16} However below are some of the polymers and coating materials specifically used for microencapsulation of Celecoxib,

- Polyvinyl pyrrolidone (PVPK 30, PVP)
- Cyclodextrin
- Poly (lactic-co-glycolic acid) (PLGA)

- Hydroxy propyl methylcellulose acetate succinate
- Polyethylene glycol and Polyvinyl alcohol
- Pluronic
- Chitosan
- poly- ϵ -caprolactone (PCL)
- Polymethacrylate (PMA) or Eudragit

Polyvinyl pyrrolidone

Polyvinylpyrrolidone (PVP), also called polyvidone or povidone, is a biodegradable, water-soluble polymer, derived from its monomer *N*-vinylpyrrolidone. In addition to being a hydrophilic polymer, PVP has excellent solubility in solvents of different polarities, good binding properties, and a stabilizing effect for suspensions and emulsions. PVP is a biocompatible and non-toxic polymer; indeed, it was also recognized as safe by the Food and Drug Administration (FDA). For this reason, in addition to the food sector, PVP is widely used in medicine and cosmetics, for pharmaceutical and biomedical applications. PVP has unique physical and chemical features, e.g., it is essentially chemically inert, colourless, temperature-resistant, and pH-stable. The various molecular weight PVPs are distinguished by different K-values, e.g., K12 (3100–5700 Daltons), K17 (7900–10,800 Daltons), K25 (23,000–32,000 Daltons), K30 (35,000–51,000), and K90 (900,000–1,300,000 Daltons).^{R-17}

Cyclodextrin

Cyclodextrins are chemically and physically stable macromolecules produced by enzymatic degradation of starch. They are water-soluble, biocompatible in nature with hydrophilic outer surface and lipophilic cavity. They have the shape of truncated cone or torus rather than perfect cylinder because of the chair conformation of glucopyranose unit. Due to superior solubilizing and complexing abilities exhibited these are nowadays most preferred for complexation and, they offer the advantage of amorphous state and complexation without toxic effects.^{R-18}

Poly (lactic-co-glycolic acid) (PLGA)

Polyester PLGA is a copolymer of poly lactic acid (PLA) and poly glycolic acid (PGA). It is the best-defined biomaterial available for drug delivery with respect to design and performance. Poly lactic acid contains an asymmetric α -carbon which is typically described as the D or L form in classical stereochemical terms and sometimes as R and S form, respectively. The enantiomeric forms of the polymer PLA are poly D-lactic acid (PDLA) and poly L-lactic acid (PLLA). Due to the hydrolysis of PLGA, parameters that are typically considered invariant descriptions of a solid formulation can change with time, such as the glass transition temperature (T_g), moisture content and molecular weight. The effect of these polymer properties on the rate of drug release from biodegradable polymeric matrices has been widely studied. The change in PLGA properties during polymer biodegradation influences the release and degradation rates of incorporated drug molecules.^{R-19}

Hydroxy propyl methylcellulose acetate succinate

HPMCAS has been used in enteric film coating of tablets and multiparticulates. For aqueous film-coating formulations, a dispersion of HPMCAS fine powder and triethyl citrate (as a plasticizer) in water is commonly utilized. Organic solvents can also be used as vehicles for applying this polymer as a film coating. However, today HPMCAS is the most widely utilized amorphous solid dispersion polymer for drug solubilization. It is most easily used via spray drying, but hot-melt extrusion is also becoming increasingly common. ^{R-20}

Polyethylene Glycol and Polyvinyl Alcohol

Polyethylene Glycols (PEGs) are semicrystalline polymers used extensively in the SDs preparation for their wetting, solubilizing, and surface active properties (Craig 1990). They have been reported to enhance the solubility, dissolution, and bioavailability of many poorly water-soluble drugs using various techniques including melting agglomeration and melting. ^{R-21} Poly (vinyl alcohol) (PVA) is a water-soluble synthetic polymer used in the manufacture of paper, textiles, and in a variety of coatings. PVA is colourless (white) and odourless, being easily biodegradable ^{R-22} PVA, a highly polar, nontoxic, water-soluble synthetic polymer prepared by the hydrolysis of polyvinyl acetate, is used in polymer blends with natural polymeric materials. Furthermore, it is utilized for a variety of biomedical applications, because of its inherent non-toxicity, non-carcinogenicity, good biocompatibility, and desirable physical properties. ^{R-23} And the combination of PVA and PEG were also used for microencapsulation and one such example is Kollocat IR

Pluronic

Pluronic represent an important class of biomedical polymers. They are unique materials composed of triblock PEO–PPO–PEO copolymers of poly(ethylene oxide) (PEO) and poly(propylene oxide) (PPO). The Pluronic PEO block is hydrophilic and water soluble while the PPO block is hydrophobic and water insoluble. In an aqueous environment, these block copolymers self-assemble into micelles with a hydrophobic PPO centre core and a hydrophilic PEO outer shell that interfaces with water. Since these micelles are amphiphilic, they are able to accommodate lipophilic molecules in the central hydrophobic core area. Consequently, Pluronic micelles are effectively used as drug carriers because their assemblies can act as passive drug containers. These assemblies deliver drugs into subcellular compartments by slowly releasing hydrophilic–hydrophobic encapsulated excipients into physiological fluids. ^{R-25}

Chitosan

Chitosan, poly(b-(1-4)-D-glucosamine), is a water-soluble product obtained by N-deacetylation of chitin. Chitin is a naturally occurring polysaccharide and second to polysaccharides as the most abundant natural polymer. Although water soluble, chitosan can be formed in different shapes such as nanoparticles, microspheres, membranes, sponges, rods, beads, and solutions. The chitosan microspheres were found to be a very favourable form for parenteral controlled

drug-delivery systems requiring low-acting drug delivery to the systemic circulation, as well as for active or passive targeting to the treatment sites. Several types of active reagents, such as DNA, Cyclosporine A, and insulin, have been encapsulated in chitosan nanoparticles. ^{R-25}

poly-ε-caprolactone (PCL)

Poly(ε-caprolactone) (PCL), a semicrystalline aliphatic polyester, is obtained by ring opening polymerization using ε-caprolactone as monomer. The PCL glass and melting temperatures are about -60C and 60C, respectively. Considering its biodegradability and biocompatibility, PCL has been studied for the development of different medical devices, tissue engineering and drug carriers as described in different review articles. Those carriers have been designed to improve the pharmaceutical properties of drugs and vaccines, to control the drug release, to enhance the drug physicochemical stability, to provide enhanced photochemical stability for the drugs, to modulate the drug skin penetration/permeation and to increase the biological (or pharmacological) responses of drugs ^{R-26}

Polymethylmethacrylate (PMMA) or Eudragit

Polymethyl-methacrylate (PMMA) copolymers are of special interest and will be the focus of this review. PMMA has demonstrated its potential to act as a drug carrier based on its biocompatibility, functionality, nontoxicity, and low cost. PMMA polymers are based within a broader family of acrylic polymers, which are typically prepared by free-radical polymerization to develop synthetic, linear copolymers.

Conclusions

Encapsulation technology has been used to provide active pharmaceutical ingredients (APIs), food ingredients, cosmetics, veterinary, hygiene, and cleaning products for decades, to name a few in Pharmaceutical industries are solvent evaporation, in-situ and matrix-polymerization, Spray drying, pan coating, fluid bed coating, extrusion, ionotropic gelation, coacervation, solvent emulsion, extrusion, high-pressure homogenization, are among the most prominent technologies utilised in the development of API delivery systems. For specific drug molecules like Celecoxib which has major challenge of solubility, various polymers and microencapsulation method have been used. From the above examples discussed, spray drying is the common microencapsulation method employed for microencapsulation of Celecoxib and some of the advantages of spray-drying include its ability to be fully automated and continuous. Other advantages are short residence times and suitability for both heat-sensitive and heat-resistant sample. General parameters used for spray drying of Celecoxib are;

- Drying gas inlet temperature: 43 to 105° C
- Dryer outlet temperature: 30 to 70° C
- Solution Flow rate: 5 to 6 ml/min
- Drying gas / air flow rate: 35 to 50 m³/hr
- Atomization air pressure or Nozzle pressure: 1 to 2kg/cm²
- Generally 2 to 5% of celecoxib

For coating polymers would be considered based on physical properties such as solubility, capacity of the core to be surrounded by the wall material, and physical properties like melting point, glass transition temperature, crystalline degree and rate of degradation etc. The coating material or the polymers should be capable of forming a film that is cohesive with the core material and there are many other parameters need to be considered for selection of coating materials. The basic studies on microencapsulated Celecoxib drug are solubility studies, size measurement of microencapsulated Celecoxib by microscopy, Dissolution studies of drug, characterization of polymers by thermal analytical techniques are very essential for the study of microencapsulation of Celecoxib or any drug molecule.

Conflict of Interest

The authors reported no potential conflict of interest.

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