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PREPARATION AND EVALUATION OF BISMUTH SUBSALICYLATE PICKERING EMULSION USING JANUS PARTICLES

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1. INTRODUCTION

1.1 Emulsions

Definition

An emulsion is a thermodynamically unstable system consisting of at least two immiscible liquid phases one of which is dispersed as globules in the other liquid phase stabilized by a third substance called emulsifying agent.

- The dispersed phase is known as the internal or discontinuous phase
- The dispersion medium is known as the external or continuous phase

For example: In an O/W emulsion oil is in dispersed phase and water is in continuous phase. Examples of emulsions include: Milk, Mayonnaise and vinaigrettes etc.

1.2 Classification of emulsions

➢ **Based on dispersed phase**

1. ***o/w* (Oil in water*) emulsion:*** Oil droplets dispersed in water phase
2. ***w/o* (Water in oil*) emulsion:*** Water droplets dispersed in oil

➢ **Based on Size of droplets**

1. **0.2 – 50 mm:** Macro- Emulsions (Kinetically stable)
2. **0.01 – 0.2 mm:** Micro- Emulsions (Thermodynamically stable)

1.3 Types of emulsions

➢ **Simple emulsions:** Also known as macro-emulsions o/w or w/o

Diameter greater than 0.1 micro meter

➢ **Multiple emulsions:** Oil-in-water-in-oil (o/w/o)

Water-in-oil-in-water (w/ow)

- **Micro emulsions:** Also known as Nan-emulsions

These are thermodynamically stable, optically transparent, Mixtures of bi-phasic oil-water system stabilized with surfactants.

1.4 Pickering emulsion

1.4.1 Definition: A *pickering emulsion* is an emulsion that is stabilized by solid particles (colloidal silica, magnesium dioxide particles, starch particles etc.) which adsorb on to the interface between the two phases. This type of emulsion was named after S.U.PICKERING, who described the phenomenon in 1907.

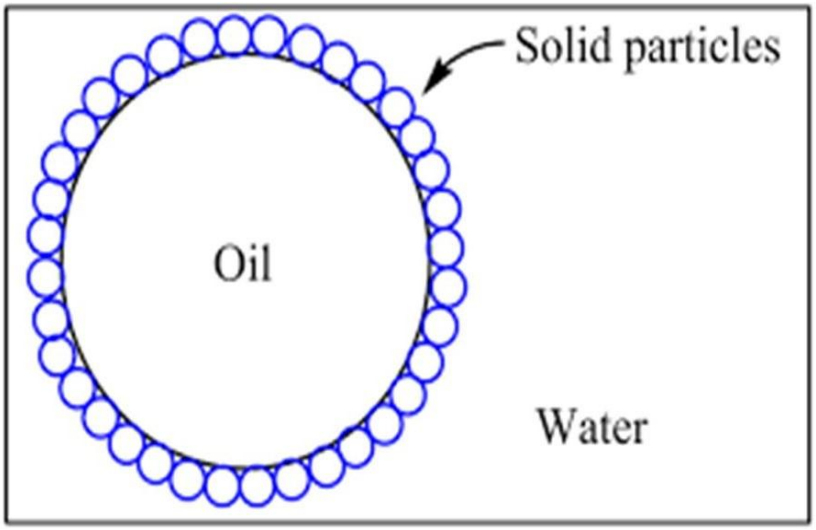


Figure 1.1: Combination of water, Oil and Solid particles makes "pickering emulsion".

Pickering emulsions are surfactant-free emulsions, stabilized by colloidal particles. These systems are experiencing renewed interest on the one hand, because it is preferable to limit the use of synthetic surfactants for ecological reasons, and on the other hand, because the functionalization of particles has undergone recent advances. It is possible to make very simple calibrated emulsions of controlled size, exploiting a phenomenon called "limited coalescence".

1.4.2 Advantages of pickering emulsion

- Solid particles reduce the possibility of coalescence , bringing about higher stability to emulsions
- These type of emulsions avoid the use of surfactants which will cause gastric irritations
- High interfacial area
- Easy catalyst, recyclability and reusability

- Avoid the use of solvents for extraction / purification steps
- Protect enzymes that deactivate easily
- Avoid accumulation of unstable intermediates
- Perform reactions that cannot be done otherwise
- Carry out multi step cascade reactions
- Water purification and protein recognition

1.4.3 Dis-advantages of pickering emulsions

- Poor hydrophobicity
- Large particle size
- Cannot be well absorbed on oil-water interface
- The effect on the emulsification of Pickering emulsion is poor
- It may also have poor stability as the emulsions are thermodynamically unstable
- **It** may show drastic effect on particle- particle interactions
- Curvature effects can be seen as it is responsible for droplet stability

1.4.4 Preparation methods of pickering emulsions

All emulsification processes used to prepare emulsions stabilized by surfactants can be applied to prepare Pickering emulsions. However, rotor-stator homogenization, high-pressure homogenization and sonication are the most commonly used to formulate Pickering emulsions. Recently, techniques such as membrane emulsification and microfluidic emulsification were also applied to Pickering emulsion preparation.

- **Rotor-stator homogenization**

A rotor-stator homogenizer simply consists of a rotor with blades and a stator with openings. As the rotor rotates, a depression is created, drawing the liquid in and out and resulting in liquid circulation. The droplet size of the dispersed phase is reduced because of the high liquid acceleration and of the shear force occurring between rotor and stator. The rotation speed and the homogenization time are the first parameters for the control of the emulsion droplet size with a rotor- stator homogenizer. In most publications, the speed of the rotor-stator homogenizer is given in rpm (revolution per minute) which is not an indicator of power. Thus, in the case of Pickering emulsions, the rotation speeds are mostly in a range from 5 000 to 30 000 rpm (corresponding to a velocity of 5 to 20 m/s when calculation is possible), while the emulsification times range from 30 s to a few minutes.

Figure 1.2: Rotor- stator homogenizer.

Advantages of rotor-stator homogenizer

- The low operating cost and the ease of setting-up which only requires to plunge the probe of the rotor-stator in the container of the three components of the emulsion
- The rapidity of the process which typically takes a few minutes to obtain an emulsion
- The small amount of liquid required, with the possibility to use only a few ml (for a preliminary test with expensive components for example)
- The existence of rotor-stator apparatus available for each step of an emulsion development, from the laboratory to industrial scales.

Drawbacks

- A possible lack of uniformity of the homogenized sample, especially when operating near the limit volume of the probe used, but which can be overcome by moving the probe around inside the sample during homogenization)
- The risk of temperature increase that is mostly due to frictional forces during the process, which can induce the destabilization of temperature-sensitive particles and/or of the emulsion (to avoid this effect, the sample can be cooled during homogenization)
- The limited energy input which limits the formation of small droplets (generally, the droplets formed with a rotor-stator are above 1 µm)
- The broad droplet size distribution obtained
- The high shear rate occurring between the rotor and the stator, which can destabilize or deform fragile particles or aggregates during the emulsification process

- **High-pressure homogenization**

This technique consists of a high-pressure pump and a homogenizing nozzle. A step of pre-emulsification to obtain a primary coarse emulsion is recommended to obtain, afterward, a fine emulsion at the outlet of the homogenizer. This pre-emulsification step is often performed with a rotor-stator or with a vortex mixer. The particles can be introduced at this step or at the inlet of the fine emulsion. Then, the pressure increases thanks to a high-pressure pump and the pre-emulsified mixture is injected in a homogenizing nozzle of small size which disrupts the drops, inducing emulsification. Various homogenizing nozzles exist and can be coupled with a high-pressure pump to form a high-pressure homogenizer. For Pickering emulsions, the pressure values are commonly in the range from tens to hundreds of MP.

Moreover, it is possible to pass the emulsion through the homogenizer repeatedly to reduce the droplet size even further down to the nan-meter range. The number of cycles through the homogenizer for Pickering emulsion formation is not always provided by authors. When information is given, it is often in the range from 1 to 10. With these parameters, the droplet sizes of the obtained Pickering emulsions range from hundreds of nano-meters to hundreds of micro-meters. The emulsion droplet size can be controlled, during the emulsification process, by both the pressure value and the number of homogenizing cycles.

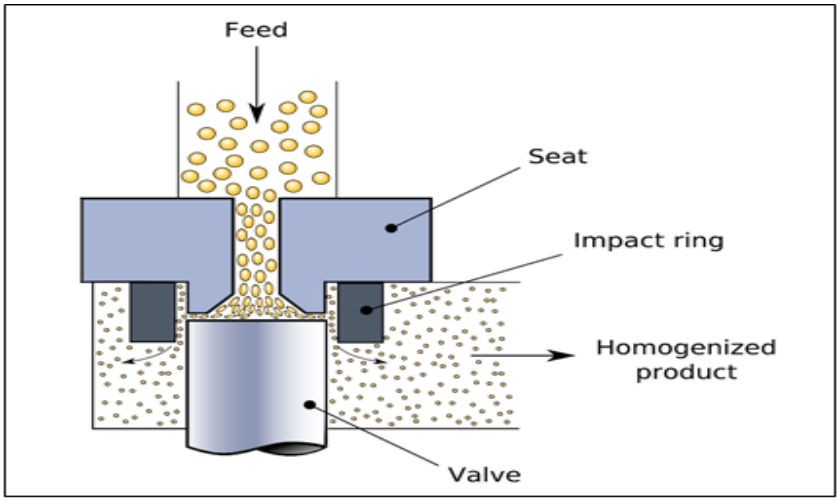


Figure 1.3: High speed homogenizer.

Advantages of high pressure homogenization

- The ability to process large volume samples in a continuous and reproducible manner
- The possibility to obtain very small droplets, even down to hundreds of nano-meters

- The possibility to tune the droplet size by increasing the pressure value or the number of homogenizing cycles.

Drawbacks of high-pressure homogenization

- The energy consumption inducing a high running cost
- The minimum volume needed, which is of tens of millilitres (larger than with rotor- stator homogenizer), also inducing a high cost for emulsions with expensive components
- The difficult cleaning, which can induce cross-contamination
- The risk of damage to the high-pressure homogenizer that can be caused by highly abrasive particles.

- **Ultrasonic-emulsification**

Ultrasounds are characterized by a frequency above 16 kHz. Only high power ultrasounds, with a frequency between 16 and 100 kHz (and to a lesser extent those between 100 kHz and 1 MHz), are able to interact with matter and can be used for emulsification. Various types of ultrasonic devices exist, the most commonly used for Pickering emulsion preparation is the ultrasonic probe. A titanium probe vibrates due to a transducer that contains a piezoelectric crystal, which converts the electric energy to very high-frequency mechanical motion. The probe transmits the ultrasonic energy to the surrounding sample, inducing the emulsification mostly by cavitation and ultrasonic forces. The ultrasound frequency and amplitude, as well as the emulsification time, are the major parameters influencing the droplet size.

Advantages of ultra-sonification

- The ease of setting up the process, which only requires lowering the ultrasonic probe in the vessel containing the three components of the emulsion
- The rapidity of the process which usually takes a few minutes to obtain an emulsion
- The small amount of liquid required to use the technique, with the possibility to use only a few millilitres (for preliminary tests with expensive components for example to be considered)
- The possibility to prepare Pickering emulsions with droplets of nanometre size of emulsions

Drawbacks of ultra-sonification

- The risk of trace amounts of titanium deposition into the sample, which can be a problem in the case of pharmaceutical Pickering emulsions

- The risk of fragile particle or particle aggregate disruption during 10 emulsification, as with the two previous processes presented above.
- The difficulties to use this technique for an industrial scale-up
- The broad droplet size distribution obtained
- The important temperature increase during the emulsification process, which can be a problem for thermo-sensitive particles or emulsion stability.

- **Membrane-emulsification**

The membrane emulsification method is a drop-by-drop technology.[108] The two main types of membrane emulsification techniques are the direct membrane emulsification (DME) and the premix membrane emulsification (PME). In the DME, the dispersed phase is pressed or injected through a micro- porous membrane into the continuous phase. The same principle is applied to the PME, except that it is the pre-emulsified mixture that is pressed through the membrane.

Techniques derived from the DME principle using low shear forces acting on the surface of the membrane to detach the droplets are also used, such as the stirred-cell membrane emulsification (SCME), the rotational membrane emulsification (RME), the vibrational membrane emulsification (VME) and the cross-flow membrane emulsification (XME). For the SCME an additional mechanical agitation is applied in the receptor chamber. For the RME and VME, the dispersed phase is pressed through, respectively, a rotating or a vibrating membrane in the continuous phase. For the XME, the dispersed phase is pressed through a membrane tube in a flowing continuous phase. In all cases, the agitation causes the detachment of the droplets from the membrane, and thus induces a smaller droplet size.

Advantages of membrane emulsification

- Being a well-suited technique for shear-sensitive products: as the shear is low, there is no risk of disruption for sensitive particles or particles aggregates
- Producing small, size-controlled and uniform emulsions with low poly-disparity
- Consuming low energy, inducing a low running cost
- Producing no heat during the emulsification process, and thus limiting the risk of destabilization for thermo-sensitive particles and emulsions.

Drawbacks of membrane emulsification

- It is time-consuming.

- It is suitable for low viscosity systems only (the system should be able to be pushed through the membrane)
- This system is presently not suitable for industrial scale-up, even if parallelization is considered.

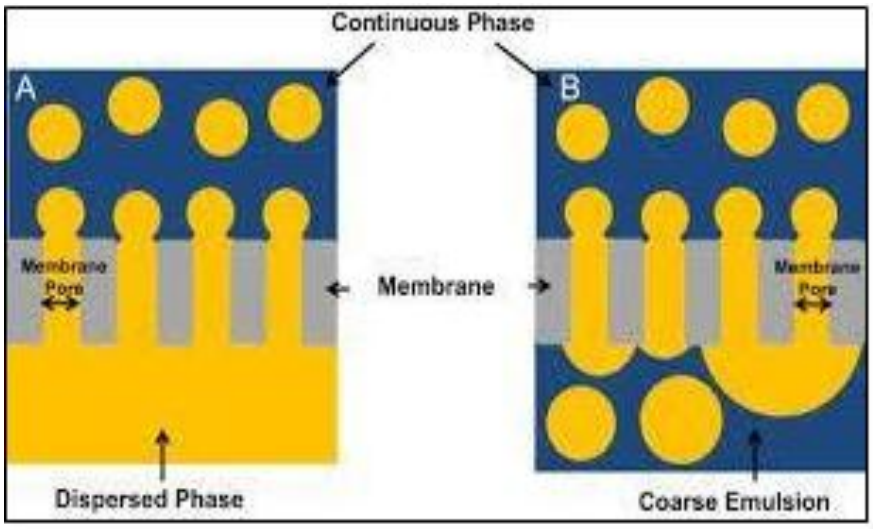


Fig. 1.4: Membrane emulsification.

- **Micro-fluidic devices**

Microfluidic devices consist of a micro-meter size channel with a particular geometry in which fluids are circulating. They allow the formation of droplets of liquid in another liquid, and thus to produce emulsions. Indeed, in laminar flow, droplets are deformed and broken by simple shear flow or elongation flow. Droplet break-up results from extension, tip streaming or trailing. Several microfluidics devices are able to produce emulsions, such as T-junction devices in which the dispersed phase is forced to flow through a small orifice into the perpendicular flowing continuous phase.

Flow focusing devices in which the flowing dispersed phase is focused by two perpendicular streams of the continuous phase from both sides, inducing the formation of a jet and then of droplets, and terrace (or plateau) devices in which the dispersed phase, surrounded by the continuous phase, circulates in a restricted micro-channel with a step. Once arriving at the step, the Laplace pressure is reduced, inducing the formation of droplets. All these microfluidic devices can be used to prepare Pickering emulsions. However, to avoid coalescence in the system, sufficient time is needed for the droplets to be covered by particles before encountering other droplets.

Advantages of micro-fluidic devices

- There is no extensive mechanical shear, and thus no significant disrupting effect on fragile particles or on particle aggregates during emulsification
- An excellent control of droplet size is achieved with an even better mono-dispersity (typically with coefficient of variation below 5%) than with membrane emulsification and, therefore, than with homogenization techniques
- The low energy consumption induces a low running cost
- A small amount of liquid is required
- There is no heat production during the emulsification process, and thus no risk of destabilization for thermo-sensitive particles and emulsion.

Drawbacks of micro-fluidic devices

- The low preparation flux which leads to a low-throughput production, which can be a problem for a potential industrialization
- The risk of interaction between the droplets and the channel
- The limitation to liquids with low viscosities able to flow through the micro-channel.

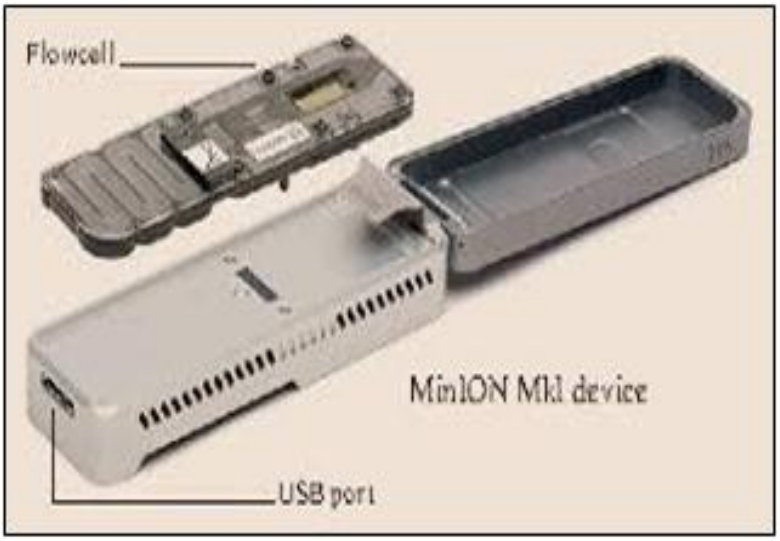


Fig. 1.5: Micro-fluidic devices.

1.4.5 Applications of pickering emulsions

In the pharmaceutical field, oral delivery accounts for 50% of the dosage forms, parenteral for 25% and topical for 10%. For emulsions, this repartition is completely changed as 55% of dosage forms are parenteral, 30% are topical and only 5% are oral. Among topical emulsions, creams are the most popular and commonly used. Until now, studies performed on Pickering emulsions are mostly fundamental works aiming to better understand the stabilization

mechanisms or the parameters influencing the emulsion properties.

- Already used in crude oil recovery, oil separation, cosmetic preparation and waste water treatment
- Convenient model system for solid particles at liquid – Liquid interfaces
- Utilization of self – Assembly
- Generate well defined three – Phase system for evaluation of particle interactions
- Easily changeable interfacial properties
- Visualization of 2D particle diffusion

A wide range of inorganic and organic biocompatible particles was studied to stabilize either O/W or W/O emulsions. Both, organic and inorganic particles can be biocompatible but only organic particles can be biodegradable. Moreover, inorganic particles might be able to cross biological barriers and accumulate, over time, in the human body inducing adverse effects. For this reason, in this part devoted to Pickering emulsions with potential interest for pharmaceutical applications, we only focused on emulsions stabilized with biocompatible and/or biodegradable organic particles.

1.5 Differences between emulsion and pickering emulsion

An **emulsion** is mixture of two liquids that would not normally mix. That is to say, a mixture of two immiscible liquids. By definition, an **emulsion** contains tiny particles of one liquid suspended in another whereas, **Pickering emulsions** are solid micro- particles or nanoparticles that localize at the interface **between** liquids are used as stabilizers, instead **of** surfactants, to enhance the droplet lifetime.

Traditional emulsion	**Pickering emulsion**
Stabilized by emulsifying agent For example : SDS, SLS Can be stable for longer period of time but it may cause toxicity.	Stabilized by solid particles For example : silica High stability, low toxicity due to presence of biocompatible polymeric adsorbents.

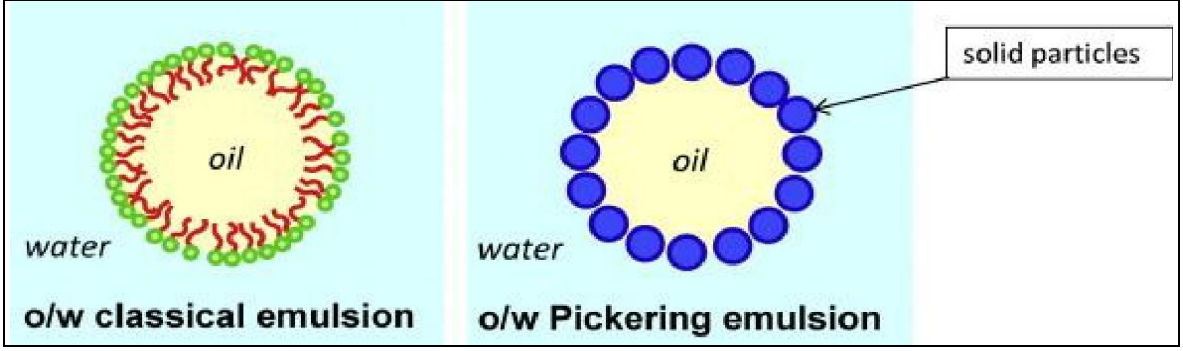


Fig. 1.6: Difference between o/w and w/o Pickering emulsion

1.6 Janus particles

1.6.1. Definition: Janus particles are special types of micro-particles whose surfaces have two or more distinct physical properties. This unique surface of Janus particles allows two different types of chemistry to occur on the same particle. The simplest case of a Janus particle is achieved by dividing the particle into two distinct parts, each of them either made of a different material, or bearing different functional groups.

For example: A Janus particle may have one-half of its surface composed of hydrophilic groups and the other half hydrophobic groups, the particles might have two surfaces of different colour, fluorescence, or magnetic properties. This gives these particles unique properties related to their asymmetric structure and or functionalization.

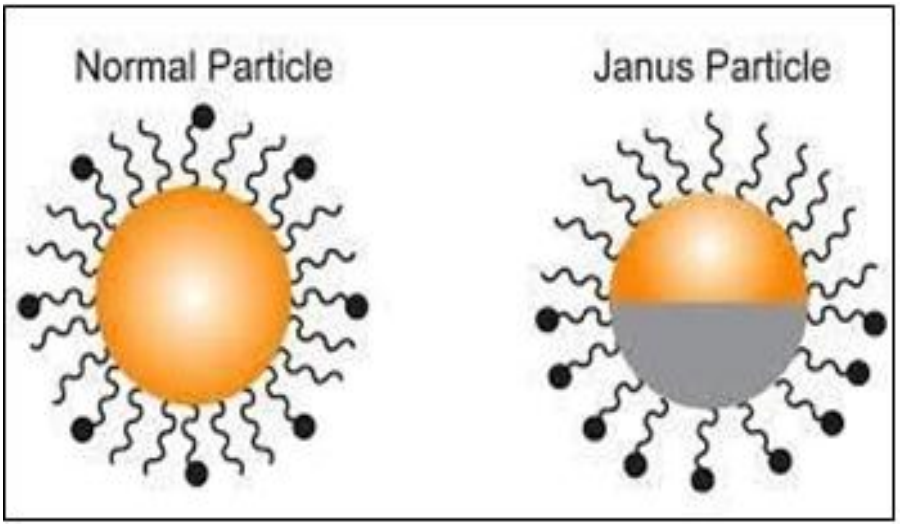


Fig. 1.7: Two- faced particles – janus particles.

1.6.2 Highlights

- Janus particles micro particles potentially useful as a building blocks for engineered materials.
- Prepared by : self-assembly of block copolymers or incompatible mixed ligand systems
- Masking with functionalization of exposed faces
- Phase separation of multi component mixtures
- Exhibit unique self-assembly properties and stabilize Pickering emulsions
- Promising for many biological applications
- Very trending technology : Janus particle technology

1.6.3 Methods of preparation of janus particles

The synthesis of Janus nanoparticles requires the ability selectively create each side of a nano-meter sized particle with different chemical properties in a cost-effective and reliable way that produces the particle of interest in high yield. Initially, this was a task, but within the last 10 years, methods have been refined to make it easier. Currently, three major methods are used in the synthesis of Janus nanoparticles.

They are however mentioned as below:

- **Masking**

Masking, as the name suggests, involves the protection of one side of a nanoparticle followed by the modification of the unprotected side and the removal of the protection. Two masking techniques are common to produce Janus particles, evaporative deposition and a technique where the micro particle is suspended at the interface of two phases. However, only the phase separation technique scales well to the micro scale. The phase interface method involves trapping homogeneous nanoparticles at the interface of two immiscible phases. These methods typically involve the liquid–liquid and liquid–solid interfaces.

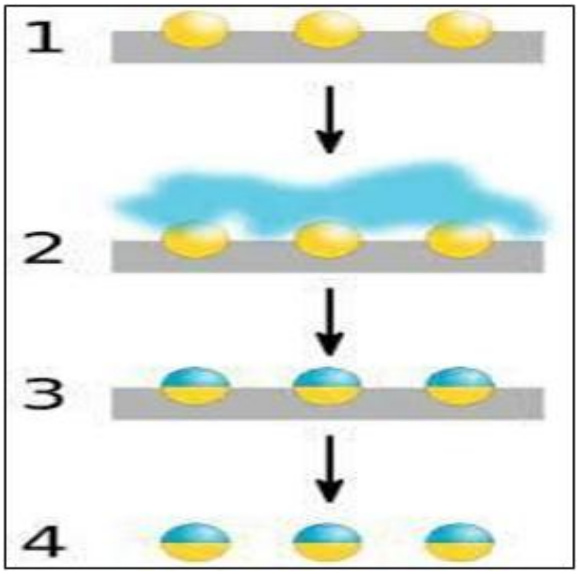


Fig. 1.8: Masking method.

A schematic representation of synthesis of Janus particles via masking

1. Homogenous micro- particles are placed in or on the surface in such that only one hemisphere is exposed
2. The exposed surface will get exposed to chemicals.
3. Due to exposure of chemicals , the particles will change its physical or properties

4. The masking agent is then removed releasing the Janus particles

- **Self – assembly**

Synthesis of Janus particles by self-assembly via block copolymers was first described in 2001 by Erhardt. They produced a tri-block polymer from poly-methyl acrylate, polystyrene and low-molecular-weight poly--butadiene. The polystyrene and poly-methyl acrylate formed alternating layers in between which poly-butadiene sat in micro sized spheres.

The blocks were then cross-linked and dissolved in THF, and after several washing steps, yielded spherical Janus particles with polystyrene on one face and poly-methyl acrylate on the other, with a poly-butadiene core. The production of Janus spheres, cylinders, sheets, and ribbons is possible using this method by adjusting the molecular weights of the blocks in the initial polymer and also the degree of cross-linking. The schematic representation along with the blocking of copolymers is as given below along with the diagrammatic representation

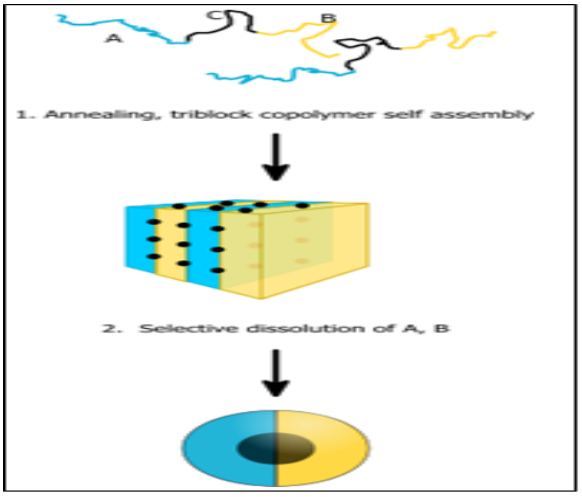


Fig: 1.9: Self assembly method.

Schematic representation of synthesis of Janus particles using block copolymer of self – assembly method.

- **Phase- seperation**

This method involves the mixing of two or more incompatible substances which then separate into their own domains while still part of a single micro particle. These methods can involve the production of Janus micro particles of two inorganic, as well as two organic, substances. Typical organic phase separation methods use co-jetting of polymers to produce Janus micro particles. This technique is exemplified by the work of Yoshi , to produce Janus

micro particles where one hemisphere has affinity for human cells, while the other hemisphere has no affinity for human cells.

This was achieved by co-jetting polyacrylamide/poly (acrylic acid) copolymers which have no affinity for human cells with bio-tinylated polyacrylamide/poly(acrylic acid) copolymers, which when exposed to streptavidin-modified antibodies, obtain an affinity for human cells.

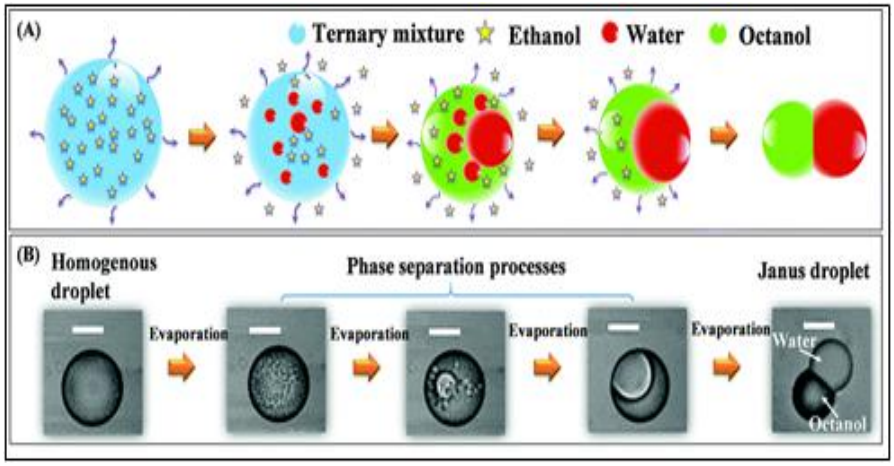


Figure 1.10: Schematic representation of phase separation process.

- **Single emulsion method**

The oil phase was created by dissolving 2.5% w/v of each *Poly glycolic acid polyethylene* glycol in 4 ml of *chloroform.* Separately, a 10ml of solution of 1%w/v poly vinyl pyrrolidine in deionized water was prepared. Whichis as follows:

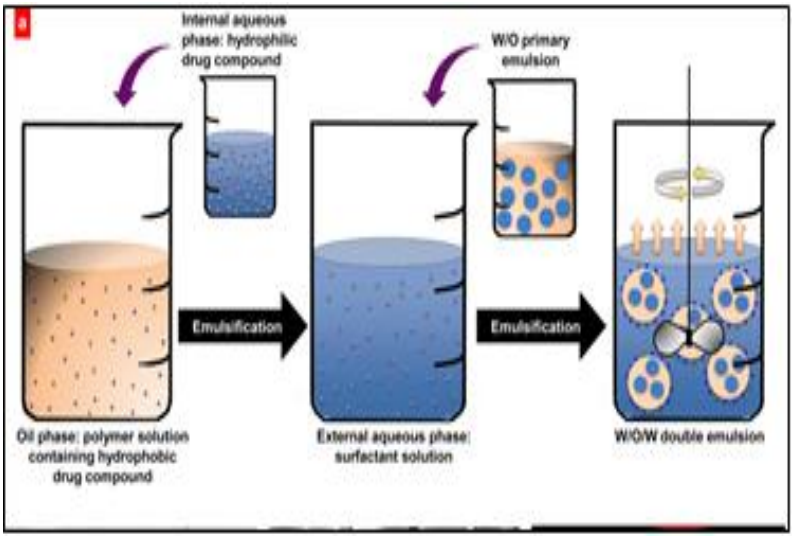


Figure 1.11: Single emulsion method.

The oil phase is added to the water phase and emulsified. The o/w emulsion was further

homogenized using a high pressure homogenizer. Post homogenization, the emulsion was kept at 40 degree centigrade in an open beaker to allow for solvent evaporation. The micro-particles were obtained.

- **Seeded polymerization**

Controlled nucleation and growth of two immiscible or incompatible polymers or a polymer and an inorganic material also may be utilized to produce Janus particles. Due to the fact that many polymers are immiscible with each other and inorganic materials may readily be functionalized to be further incompatible with polymers, the direct phase separation method is suitable for a wide range of materials.

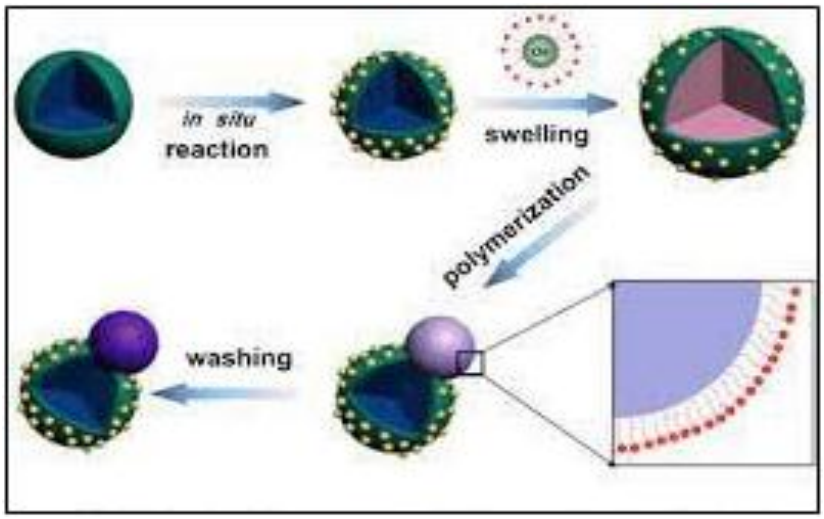


Figure 1.12: Seeded- polymerization.

Seeded polymerization was originally used for the production of core- shell particles. However, it was discovered that under the right conditions and with sufficient incompatibility of the monomer and seed polymer, heterogeneous nucleation becomes favourable. In this approach, cross-linked polymer seed particles are swollen with polymerizable monomer. The monomer is polymerized upon heating. The cross-linked polymer network then shrinks and ejects the monomer solution, forming a bulge on the particle surface.

Seeded emulsion polymerization is most frequently applied to organic-inorganic hybrid anisotropic particles that incorporate silica or iron oxide along with a polymer such as polystyrene (PS). Typically, these structures have one major component and one minor component. High yields of Janus particles in the nano-scale particle size range have been synthesized using the seeded polymerization methods.

1.6.4 Advantages of janus particles

Biphasic Janus particles hold great promise as sophisticated drug delivery systems with the potential to solve many fundamental problems in drug delivery. Co-encapsulating two synergistic drugs in a single particle is the only way to ensure co-localization of both drugs at the same time. The ability to deliver multiple therapeutic agents in a single platform with independent release kinetics allows for unprecedented control over the order and rate at which each compound is released. As with other micro carriers, the rate and onset of drug release is determined by the degradation behaviour of the polymer matrix. Janus particles can also deliver both a therapeutic agent and an imaging modality to enable real time tracking of treatment.

The incorporation of stimuli-responsive polymers imparts an even greater degree 5 of flexibility in the design of Janus particles; for example, one or both compartments could be designed to degrade in a pH-dependent manner so as to prevent degradation or drug loss during various stages of digestion, or, alternatively, to trigger drug release in an acidic tumor microenvironment . Furthermore, zero-order release has been demonstrated with a hemi-spherical particle that only allows degradation on the face. Therefore, Janus particles comprised of one biodegradable polymer and one non- biodegradable polymer (i.e., PLGA and PMMA) could potentially mimic this system, enabling zero-order release. Due to the difference in chemical composition of the two halves, each compartment will intrinsically exhibit a unique release.

1.6.5 Bio-medical applications of janus particles

The potential application of Janus particles in different fields is only emerging, and is probably limited only by our imagination. As a multifunctional nanomaterial, the intrinsic appeal of Janus particles is their unable and controllable asymmetric structure, which allows for spatially controlled functionalities down to the micro scale. This is particularly attractive for biomedical applications because of the synergistic potential for multiplexing, multi-level targeting, and combination therapies. A few examples below highlight these possibilities In drug and gene delivery, targeting is vital to spare healthy cells from damage and to enhance the bioavailability of the drug. Current controlled release particles use conjugated ligands on the surface of the particles for targeting. It may be advantageous to decouple the targeting function from the therapeutic function in the same particle.

1.6.6 Janus particles for bio-imaging

Cell-based therapies (like cancer immunotherapy or stem-cell therapy), chemotherapy or photo-thermal therapy have received considerable attention in oncological research. These therapeutic strategies often require imaging technologies to track the therapeutic cells or tissues in real time. OI, CT and MRI are commonly used imaging modalities, though these techniques are not without limitation. For example, OI presents poor spatial resolution and tissue attenuation. CT and MRI are only efficient in detecting tumors larger than 0.5 cm and show low sensitivity. Therefore, developing a nano- platform to act as contrast agents for multi-imaging techniques would be highly beneficial for cell labelling and in vivo imaging. JPs that combine different functional materials into a single unit, capable of diverse composition and surface chemistry, have been shown to exhibit excellent performance in multi-modality imaging.

1.6.7 Janus particles for bio – sensing

Biosensors that are capable of multiple functions, i.e. simultaneous detection of many diverse analytes and that also display separation, enrichment, signal transduction characteristics, have attracted increasing attention Considerable effort has been made to construct multiple nanostructures with multifunctional properties, such as core-shell particles . However, additional coatings or modification will decrease these specialist properties. In contrast, the unique morphology of JPs make superior candidates for multifunctional biosensor construction. Recently, a variety of JNPs have been reported as biosensors for bio-molecular detection. For example, Lu fabricated a multifunctional bio-sensing platform composed of hematite-silica hybrid of Janus γ- Fe2O3/SiO2 nanoparticles (JFSNs) for sensitive colorimetric detection of glucose.

1.7 Bio-pharmaceutical aspects

The ability of lipids to enhance the bioavailability of poorly water soluble drugs has been comprehensively reviewed. They are as given below

- For highly lipophilic drugs, lipids may enhance the bioavailability directly or indirectly via a reduction in first pass metabolism
- Various combinations of lipids, lipid digestion products and adsorbents have been shown to have permeability enhancing properties

1.8 Approaches of drug delivery systems

Pickering emulsions have displayed great potential in oral drug delivery. Their unique

structure endows them with good stability, excellent biocompatibility, and environmental friendliness. Several-fold increases in the oral bioavailability or bio-accessibility of poorly soluble drugs, such as curcumin, silybin, puerarin, and rutin, were achieved by using Pickering emulsions, whereas controlled release was found for indomethacin and caffeine. The shell of the interfacial particle stabilizers provides enhanced gastrointestinal stability to the cargos in the oil core. Here, we also discuss general considerations concerning particle stabilizers and design strategies to control lipid digestion.

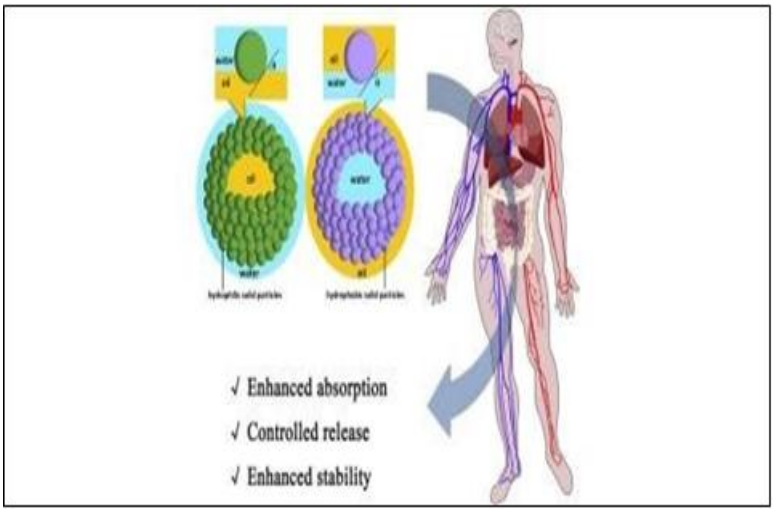


Figure 1.13: Schematic representation of drug delivery.

Highlights

- ❖ Properties of particle stabilizers are crucial to construct Pickering emulsions
- ❖ Pickering emulsions enhance bioavailability or bio-accessibility of drugs
- ❖ Controllable release and high stability relate to the interfacial particles
- ❖ Digestion can be tailored by tuning the properties of the particle stabilizers

3. AIM AND OBJECTIVES

1. Aim

Preparation and Evaluation of bismuth subsalicylate pickering emulsion by using janus particles.

Objectives

- Pre-formulation studies of drug
- Preparation of Janus particles
- Optimization of Janus particles

- Preparation of Pickering emulsions using optimized Janus particles
- Evaluation of Pickering emulsion

2. Review of literature

21 **Sidy mouhamed dieng et al,** in his work **"Formulation, Evaluation of water/oil Pickering emulsion stabilized by Mgo particles**," Used Mgo as an adsorbent which will limit the coalescence and reduces the interfacial tension, Thus, he mentioned that these dispersed systems will protect an active ingredient in the formulation. They can increase solubility, therapeutic index by decreasing toxicity and increasing efficacy. The concept of emulsions stabilized by solid particles is experiencing renewed interest today because of many advantages it present good stability, protection of environment, the safety of uses, varieties of particles etc, This study suggests that adsorbents like Mgo, tio2, can be used to stabilize the surfactant free emulsion.

22 **Marto et al and Chevalier et al**, in their work "**Pickering emulsions: Challenges and Opportunities of Topical Delivery"**, Mentioned that it is the most convenient and easiest way for drug administration. To overcome some penetration obstacles, a favoured strategy relies on selecting suitable vehicles for dermatologic therapy, such as Pickering emulsion, gels and more recently, nanoparticles system. This review focuses in delivery of drug formulated as Pickering emulsion devoted to topical delivery only.

23 **Grunning et al,** in their work "**Janus particles modified at their surface by hydrophilic and hydrophobic groups",** Mentioned that particles less than 100mm size and modified by hydrophilic and hydrophobic groups where in the hydrophilic and hydrophobic groups are distributed anisotropic ally on the surface of the modified particles. Processes are the preparation of such particles and the use of such particles as surface active products. Especially for stabilizing or destabilizing emulsions and foam as well as for tertiary oil recovery.

The Janus beads were the properties of such beads at oil/ water interfaces and point out that they do behave differently from ordinary solid particles. These observations are interpreted semi- quantitatively and open up the way to further prospects and applications to be considered.

24 **Aveyard et al,** in his work "**Emulsions stabilised solely by colloidal particles – colloidal surfaces"** Mentioned that the Pickering emulsion focused on the stabilization only by solid particles absorbed at the oil – water interface, particularly silica or magnesium nano particles that show well- controlled surface properties. The stabilization of particles depends on the polymeric structures. Emulsification of droplets surrounded by various distinct emulsions are however authorized by the emulsion properties of absorbed droplet of the free energy of the line tension in the three- phase contact angle around particles adsorbed at the droplet interface during emulsification. A positive line tension might lead to a positive free energy of particle adsorption mostly for close angles to the extent positions. The stimulations and theoretical approaches have structure and dynamics of particles to be inserted for their work and influenced by the particle- particle interactions to the session of oil – water interfaces.

25 **Hunter et al,** in his work "**The role of particles in stabilizing foams and emulsions that is stabilized emulsions"** In his work mentioned that he evaluated the stability of particle stabilized foams and emulsions to determine the similarities and difference between foam systems and emulsions. And he also discussed about the self- assembly of different materials (e.g. nano particles, nano rods and nano sheets) at fluid interfaces. They found that at fluid interfaces, self- assembly is influenced by the nano material shape, and that the nano particle interfacial assembly is mainly driven by a reduction of the interfacial energy. They obtained anisotropic nanoparticles with different orientations by controlling the bulk particle concentration.

26 **Xiao et al,** in his work "Tailoring **the wettability of colloidal particles for Pickering emulsions via surface modification and roughness"** Discussed advances in tailoring the wettability of colloidal particles for Pickering emulsions along, with the related applications. They focused on switchable Pickering emulsions with their environmental responsive properties and the effect of surface roughness. They also thoroughly described the methods to finely tune the particles wettability by modifying their surface functional groups (physical adsorption or chemical anchoring) or topology .Xiao et al. stated that tuning the wettability of small molecules or polymers offers ample opportunities for industry-related applications along with their statuses.

27 **Gleot et al ,** in his work "**Emulsification of oil and water in the presence of finely divided solids and surface – active agents"**, He observed that when the particles

concentration increases, the emulsion is stable against coalescence for a longer time because more particles an go to the interface and improve the emulsion stability. Moreover, coalescence can be prevented by covering droplets with a tightly packed layer of particles. Besides the classical arrangement of two densely packed monolayers, other particle- based structures can prevent droplet coalescence, such as dense layer of bridging particles and a layer of aggregated particles and a layer of density network. These structures typically involve some particles aggregation and droplet flocculation. The rigid structure consists of disordered network of particles that are adsorbed to the oil – water interface and are held together by attractive inter – particle forces.

28 **Binks et al,** in his work "**Compositional ripening of particle – and surfactant – stabilised emulsions: a comparison"** Showed that in Pickering emulsion mixtures, droplets coalescence is triggered by compositional ripening. Conversely, coalescence is inhibited by the addition of an excess of particles because they attach to and stabilize the liquid- liquid interface. Interestingly, particles protruding from a droplet can simultaneously adsorb to another interface, thus bridging two droplets through a shared particle monolayer. This configuration satisfies the equilibrium contact angle on both sides of the bridging particle, thus preventing coalescence. However, this is not a general rule for emulsion stability, because in some cases, an increase in the number of particles leads only to a particle excess in one liquid.

29 **Gavrielatos et al,** in his work, **"Oil/water emulsions stabilized by nanoparticles of different wettability's"** revealed that the presence of nanoparticles in an emulsion, even at very low concentration (0.005% or 0.01%) significantly increases the O/W emulsion separation time from a few minutes, (in the absence of nanoparticles) to several hours or even days. The emulsion stability typically increases proportionally with the nanoparticles concentration. It was demonstrated that the emulsion stability could be influenced by the shearing time, with longer shearing times resulting in an slow separation rates due to the dispersed droplets having a smaller size. However, this effect decreases when droplets reach the equilibrium size, and the separation kinetics will not be further retarded accordingly to the Pickering emulsions.

210 **Mwangi et al,** in his work "Effects **of environmental factors on the physical stability of Pickering emulsions stabilized by chitosan particles"** Investigated that how the stabilizing activity of self- aggregated chitosan particles is influenced by the chitosan

concentration and environmental factors (i.e. ionic strength, temperature, and pH). They found that droplet coalescence and found that droplet coalescence and creaming were prompted by progressively, decreasing the pH with the emulsification occurring at low ph. Furthermore, emulsion stability was improved by particle aggregation at the oil/water interface, and by the formation of chitosan networks in the continuous phase, which limits the droplet interactions. The emulsion stability and type can be modulated just by controlling, adjusting the pH and ionic strength. Variations in pH can dramatically modify the emulsions micro structure and properties, as well as the particles hydrophobicity and ultimately affect its stability by destroying the droplets.

2.11 **Arditty et al, in his work "Some general features of limited coalescence in solid – stabilized emulsions"** Investigated the coalescence aspects and rheological properties, of emulsions stabilized by silica particles in order to better understand the mechanisms underlying emulsion destabilization, covalent modification of silica nano particles harbouring hydrophilic and hydrophobic groups that mimic the properties of surfactants. They showed that such nano particles can be used to produce emulsions with smaller droplets compared with the smaller droplets of surfactants. Such emulsions are stable upto 1.5 years. The stability improvement that was obtained using modified silica nano particles, other researchers investigated other modifications. Thanks to their interfacial adsorption, these particles make it possible to produce o/w emulsions with small droplet sizes**.**

2.12 **Nallamalli et al, in** his work "Stabilization **of Pickering emulsions with oppositely charged latex particles: influence of various parameters and particle arrangement around droplets"** studied different variables (i.e. oil to water ratio, mixed particle composition, and pH and the demonstrated that the emulsion type and stability were related to the behaviour of the particles dispersed in the aqueous phase before emulsification. They also found that the kind of emulsion formed (i.e. droplet diameter, stability) depended on the wettability properties of the Pickering emulsions of the 2D components to be emulsified of the components, such as the interfacial behaviour of the boron nitride are largely explored components of the Janus particle preparation of the solid particles of the emulsions.

2.13 **Yan et al,** in his work "**Janus mesoporous silica nano sheets with perpendicular mesochannels: affording highly accessible reaction interfaces for enhanced biphasic**

catalysis" carried out studies based on the 2D structures of the stabilizing Pickering emulsions. They explored the ability of Janus particle meso-silica Nan sheets with perpendicular mesochannels to be used as an interfacial catalyst for biphasic reactions. The interfacial catalyst of the Janus particle Msio2 Nan sheet was examined by testing its capacity to emulsify a toluene/ water system, resulting in a well- defined w/o emulsions. The unique 2D structure showed enhanced catalytic activity in aqueous nitroarene hydrogenation reactions, which was 13 times higher than that of a conventional silica-based interfacial catalyst.

2.14 **Poggi et al,** in his work, "**Polymeric Janus nano particles template by single emulsion copolymer method",** He mentioned that he utilized self- assembled thin films of PS-b-P4VP block copolymers to template. Janus particles as can be seen in the spin- cast and solvent annealed the co-polymer to achieve vertical cylindrical of P4VP in a PS matrix. The particles were subsequently functionalized with an alkyne group, cross linked and then functionalized with an alkyne PEO brush via click chemistry. Finally, Janus particles are produced by dissolving the film in a good solvent for the PS domains. The Janus particle exploited and synthesised and coated with DNA by first immobilizing using the Janus particle preparation using the solid particles.

2.15 **Fournier et al,** in his work "**Effect of dispersed phase viscosity on solid- stabilized emulsions"** noticed that, at constant emulsification time and for a fixed amount of Janus particle, the volume of emulsified oil increased when the oil viscosity decreased. The oil viscosity is a damping factor for particles anchoring at the oil/ water interface in between them, as it slows down the particles diffusion and adsorption rate. They obtained a constant emulsion droplet size and made it stable enough for further stable emulsion that is being made evenly in the formulation of emulsions to be specified. This behaviour of particles in the Pickering emulsion was the result of combination between the both articles and subjects that are going to subject themselves in the viscosity of the particles in the Pickering emulsion preparation. The increase in the droplet coalescence and slow down of the glass particle adsorption rate at the interface along with the particle viscosity in the Pickering emulsions.

2.16 **Manga et al,** in his work "**Emulsions and their stability along with the evaluation studies",** Demonstrated that a minimum droplet size exists, even if the rotation speed still increases. This has been attributed to a competition between the particle adsorption rate at

the oil/water interface and the droplet detachment rate from the membrane. If the particles have a slow rate of adsorption at the interface, the uncovered droplets have time to coalesce before being stabilized inducing a size increase. Finally, an agitation/rotation speed increase leads to a droplet size decrease, because it induces an easier detachment of the droplets from the membrane. At low rotation speed, the shear is very low. The particle adsorption rate is also very low and considered to be very associative and conditional.

2.17 **Levine et al,** in his work "**Pickering emulsion – homogenization methods random distribution"** Noticed that, rather than having a random distribution, the weakly covered (i.e. not densely packed particles on the surface) droplets exhibited areas with close-packed particles and areas without particles. Conversely, weak coverage does not necessarily induce poor emulsion stability. They also observed that at low surface coverage, the particles adsorbed at the droplet surface were able to redistribute themselves in the contact region between droplets and to inhibit droplet coalescence. The particle aggregates, rendered more hydrophobic, stabilized preferentially W/O emulsions. In addition, the formation of multiple emulsions was observed near the inversion point.

5. Methodology

Methodology involves the preparation methods and on what basis the polymers were chosen for the preparation and evaluation of Pickering emulsion.

5.1 Preformulation studies

The most important criterion for the screening of components for the emulsion is solubility of poorly soluble drug in oils. The drug BISMUTH SUBSALICYLATE was tested for its solubility in various oils. An excess amount of drug was added into 2ml of oil in 5ml capacity vials. The samples were centrifuges at 5000rpm for 20 minutes. The supernatant was taken and filtered. The concentration of BISMUTH SUBSALICYLATE in the samples was determined using UV spectrophotometer by measuring the absorbance of samples at 256nm. We observed the physical properties like color, shape, color, solubility etc.

Various polymers like sodium alginate, carbopol and Poly Glycolic Acid (PGA) were used for preparation of Janus particles among them PGA producedstable particles. Hence PGA was selected for the further studies.

Construction of standard calibration curve

Standard calibration curve of Bismuth subsalicylate was constructed by preparing Primary stock solution of the drug using 0.1 N Hcl as solvent. From thee primary stock solution seven different drug solutions like 10 µg/ml,20 µg/ml, 30 µg/ml, 40 µg/ml, 50 µg/ml, 60 µg/ml, & 70 µg/ml were prepared and absorbance was determined by using UV Visbile Spectrophotometer at 256 nm. The results are tabulated and the Curve was drawn.

5.2 Solubility of poly-glycolic acid in various solvents

Selection of a solvent was done based upon the **Solubility studies** as it is the most important criterion for the screening of components. The solubility **Polyglycolic acid** was determined by adding an excess amount of 2.5mg of PGA in various solvents like chloroform, dicholoro-methane and hexa-flouro isopropanol. Based on the solubility studies **Chloroform**showed better Solubility of PGA, Hence it is used as solvent for the further studies and Janus particle were prepared by dissolving 2.5mg of PGAin 4ml of chloroform.

5.3 Solubility of bismuth subsalicylate in various oils

Various oils were chosen for the solubility of Bismuth subsalicylate drug such as **Castor oil, Arachis oil, and Almond oil.** Solubility studies were performed in these oils and highest solubility was found in A**rachis oil.**

So based on the solubility studies we selected **Arachis oil** for the further studies. And using Arachis oil we prepared Pickering emulsion.

5.4 Preparation of janus particles

Janus particles were prepared by using **Single – emulsion** method and the process of preparation is as follows:

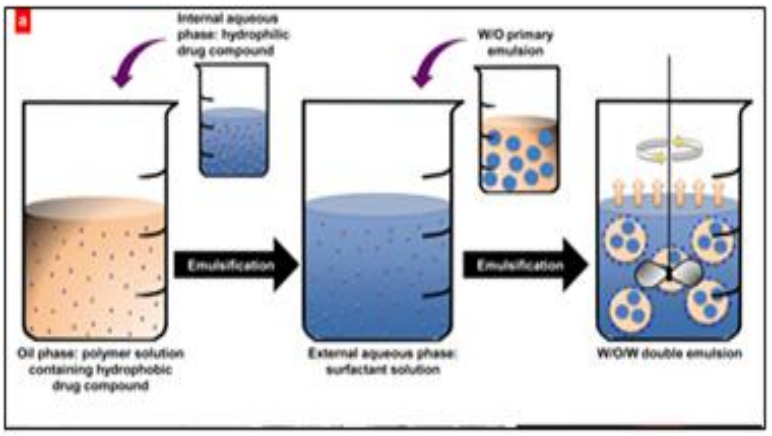


Figure 1.15: Preparation of Janus particles.

The oil phase was created by dissolving 2.5% w/v of each ***Poly glycolicacid***and *polyethylene* glycol in 4 ml of ***chloroform***. Separately, a 10ml of solution of 1%w/v poly vinyl pyrrolidine in deionized water was prepared. **(**1gm in 100ml).

The oil phase is added to the water phase and emulsified. The o/w emulsion was further homogenized using a high pressure homogenizer. Post homogenization, the emulsion was kept at 40 degree centigrade in an open beaker to allow for solvent Evaporation. The micro-particles were obtained. The solid particles were prepared and further used for the preparation of Pickering emulsion.

5.5 Preparation of pickering emulsion

Pickering emulsion was prepared with various Janus particle concentrations. Equal amounts of oil phase and water phase was taken. The **Arachis oil** was selected for this preparation of Pickering emulsion because of its drug solubility criterion.

The **Arachis oil** was preferred for the preparation of Pickering emulsion by the addition of water into it. Equal amounts of oil phase and water phase was taken. And different concentrations of Janus particles was added into it along with the **bismuth subsalicylate** drug. Shaken vigorously and kept in the homogenizer at 2000rpm for the perfect mixing of components. The solid particles reduce the interfacial tension in between the oil phase and water phase and make it a stable emulsion without any unstable properties.

So the different concentrations of Janus particles were taken and Pickering emulsion was prepared and observed for 3 days. Only the Pickering emulsion with 1.5% concentration was stable and no phase separation was found in it. Other concentrations of Janus particle showed unstable emulsion that is phase separation occurred in them, which can be visually seen in the beakers.

One of the all concentrations showed the stable emulsion properties. To know which is the best and stable emulsion, we have conducted the evaluation studies which can be seen further.

Calibration curve of Bismuth subsalicylate was plotted using various concentrations and absorbance which were observed in UV- spectrophotometer.

5.6 Evaluation studies

Various evaluation studies were performed which are as follows:

5.6.1 Viscosity determination

The principle of measuring the viscosity retained by Brookfield is based on the application of a movement force to a product by rotating at fixed speed, a fixed-size mobile. The resistance of the product to the rotational movement of the mobile is recorded using an internal spiral spring and converted to an isometric unit. In order to expand measurable viscosity ranges, several mobiles, speeds and spring types were used.

The viscosity of the emulsions was strongly influenced by the amount of Janus particles and Bismuth Subsalicylate concentrations, in the internal phase. We have found that a high concentration of Janus particle has led to an increase in the viscosity of the external phase of the emulsions. The test tube with 2g of Janus particle have a much higher viscosity than the test tube containing 1g of Janus particle. Hence the viscosity changes when the concentration of solid particles changed

5.6.2 Conductivity

The principle of conductivity measurement is based on the measurement of the electrical resistance of the solution. In a 50ml conical tube with a screw cover containing the emulsion, the Conductometric cell is introduced. The conductive cell is plunged to the level of the emulsified phase for sedimentation tubes. In the presence of a conductive solution the needle of the galvanometer deviates towards higher values.

The conductivity results are zero 0.5 mS.cm-1 throughout the monitoring period of our emulsions. Studies have shown that the conductivity of the O/W must be less than or equal to 0. 7 mS.cm-1 and the constant value of the conductivity in time is a decisive criterion of stability. Indeed, the variation in conductivity is proportional to the variation of the external phase proportion when it is an O / W emulsion and the conductivity hardly changes for changes in the proportion of a W / O emulsion.

5.6.3 PH of the emulsions

The principle is based on the measurement of the potential between two electrodes dipping in a solution rich in H + ions. After calibrating the pH meter, the combined electrode is soaked in a 50ml conical tube with screw cover containing the preparation. As with conductivity, it is necessary to ensure that the electrodes are dipped to the emulsified phase level for

sedimentation tubes. The reading time is set at 3 minutes after the electrode was introduced.
A basic character was observed for all of our emulsions. This basicity is more marked for emulsions containing 1.5g of Janus particle than for emulsions containing other concentrations of Janus particle. The Janus particles used in a powder form, with a strong basic character leading to the basicity (pH> 7) of our emulsions giving them a better stability. YANG et al showed that a basic pH improves the stability of emulsions.

5.6.4 Creaming

Separation of an emulsion into two layers, one of which is richer in the disperse phase than the other is called creaming. Creaming causes inelegancy to the emulsion and if it is not shaken adequately, the patient might obtain an incorrect dosage.

Reducing the droplet size through efficient emulsification may result in the stabilization of the emulsion by avoiding creaming. An increase in the viscosity may also help in the stabilization of the emulsion.

Various formulations with different Janus particle concentrations were prepared and observed. The various concentrations were 0.5, 1. 1.5, 2, 2.5 and 3 %. The formulations with the concentrations of 0.5,1, 2, 2.5 and 3 % of Janus particle were unstable and creaming was observed after 3 days. Only the sample containing 1.5 % of Janus particle was stable and no creaming was observed.

5.6.5 Dissolution studies

Dissolution is defined as “the amount of drug substance that goes into solution per unit time under standardized conditions of liquid / solid interface, temperature and solid solvent composition”. Dissolution is conducted to know the minimum time taken by the drug to dissolve itself in the systemic circulation and starts its action in the body.

The quantitative in vitro release test is performed in purified distilled water as dissolution medium. The dissolution test was carried out in USP apparatus – II (paddle) Pickering emulsion are placed in gelatin capsule at 70rpm and 37^0 C, during the release period to compare the release profile with marketed dosage form. Sample solutions were withdrawn at 5, 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60 minutes of time intervals. The fresh volume of the medium was replaced with the withdrawn volume to maintain the sink conditions. Samples withdrawn were analyzed for the amount of drug release. Percent drug release was calculated at different time intervals.

6. RESULTS AND DISCUSSION

6.1 Preformulation studies

6.1 Properties of bismuth subsalicylate

Table 1

S. no.	Properties	Characteristics
1.	Shape	Amorphous powder
2.	Colour	White powder
3.	Odour	Odour less
4.	Solubility	Practically insoluble in water or alcohol
5.	Melting point	350 ^{0} c
6.	Boiling point	1,564 ^{0} c

6.2 Selection of suitable solvent for polymer

6.2.1: Solubility of Poly-Glycolic acid in various solvents

Table 2

S. no.	Solvents	Solubility (mg/ml)
1.	Chloroform	18.5
2.	Di- Chloromethane	13.7
3.	Hexa-flouro isopropanol	11.6

So based on the solubility studies wehave selected**Chloroform** as a solvent for the further studies. And the Janus particle were prepared by dissolving 2.5mg of PGAin 4ml of chloroform.

6.2.2: Solubility of bismuth subsalicylate in various oils

Table 3

S. no.	Oils	Solubility (mg/ml)
1.	Castor oil	21.62
2.	Arachis oil	26.42
3.	Almond oil	18.14

The above studies suggeststhat, amongst various solvents chloroform was the best solvent for POLY-GLYCOLIC ACID and the ARACHIS OIL had the highest solubility of BISMUTH SUBSALICYLATE. Hence, was chosen as oil phase.

6.3 Formulations

6.3.1 Formulation of janus paticles

Table 4

S. no.	Components required	Volume taken
1.	Poly-glycolic acid	2.5 g in 100ml (10ml)
2.	Poly – ethylene glycol	2.5 g in 100ml (10ml)
3.	Chloroform	4ml
4.	Pvp	1 g in 100 ml (10ml)
5.	De- ionized water	10 ml

6.3.2 Formulation of pickeirng emulsion

Table 5

Components	F1	F2	F3	F4	F5	F6
Drug	5mg	5mg	5mg	5mg	5mg	5mg
Janus particles	0.5 mg	1mg	1.5mg	2mg	2.5mg	3mg
Arachis oil	10ml	10ml	10ml	10ml	10ml	10ml
Water	10ml	10ml	10ml	10ml	10ml	10ml

The different concentrations of Janus particles were taken and Pickering emulsion was prepared and observed for 3 days. Only the Pickering emulsion with 1.5% concentration was stable and no phase separation was found in it. Other concentrations of Janus particle showed unstable emulsion that is phase separation occurred in them, which can be visually seen in the beakers. The analysis of Pickering emulsions was observed with different time intervals which is as follows:

6.3.3: Changes in pickering emulsion with time

Table 6

S. no.	Time-interval	F-1 (0.5%)	F-2 (1%)	F-3 (1.5%)	F-4 (2%)	F-5 (2.5%)	F-6 (3%)
1.	After 3 hrs.	No change	No change	No change	No change	Phase separation	Phase separation
2.	After 6 hrs.	No change	No change	No change	Phase separation	Phase separation	Phase separation
3.	After one day	Phase separation	Color-change	No change	Phase separation	Phase separation	phase separation
4.	After two days	Phase separation	coalescence	No change	Phase separation	Phase separation	Phase separation
5.	After three days	Phase separation	phase separation	No change	Phase separation	Phase separation	Phase separation

So the above table suggests that the beaker containing 1.5% concentration of Janus particle was stable as compared to other formulations. Further evaluation studies were performed to

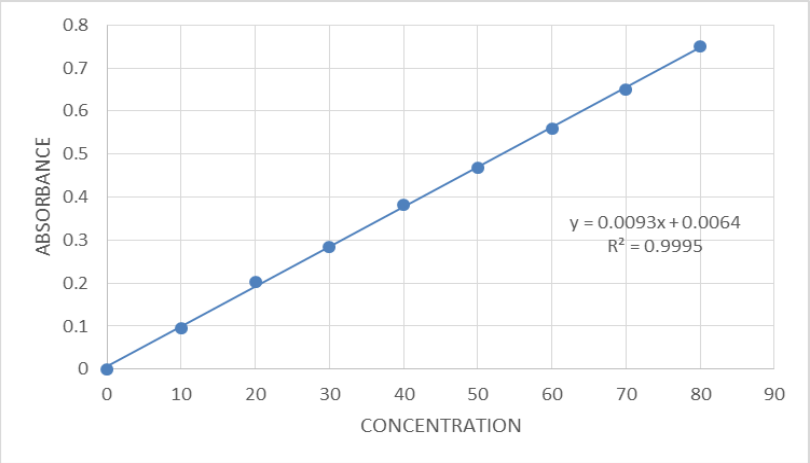
identify the stable formulation of Pickering emulsion

6.4 Evaluation studies

6.4.1. Calibration curve of bismuth subsalicylate

Table 7

S. no.	Concentration (µg/ml)	Absorbance (nm)
1	0	0
2	10	0.096
3	20	0.203
4	30	0.285
5	40	0.383
6	50	0.467
7	60	0.559
8	70	0.650



The linear Calibration Curve was obtained at concentration range 10-70 microgram / ml. With a correlation coefficient (0.9995), slope (0.0093) and intercept (0.0064).

6.4.2 Viscosity determination

Table 8

S. no.	Formulation code	Viscosity at rpm (cps)
1.	F1	19.24± 0.32
2.	F2	22.26 ±0.24
3.	F3	36.34 ±0.12
4.	F4	38.24 ±0.24
5.	F5	38.36 ±0.32
6.	F6	32..36 ± 0.53

The viscosity determination analysis is as given above in the table with various formulations as mentioned.

6.4.3 Electro-conductivity

Table 9

S. no.	Batch code	Conductivity study (ms/cm)
1.	F1	0.420
2.	F2	0.480
3.	F3	0.540
4.	F4	0.538
5.	F5	0.520
6.	F6	0.500

6.4.4 Phdetermination

Table 10

S. no.	Batch code	Ph
1.	F1	6.14
2.	F2	6.36
3.	F3	7.32
4.	F4	7.68
5.	F5	8.42
6.	F6	8.64

6.4.5 In-vitro dissolution studies

Dissolution study was performed to compare the drug release from the prepared BISMUTH SUBSALICYLATE Pickering emulsion formulations and the pure drug. The quantitative in vitro dissolution studies were carried out to assess drug- release form the oil phase into the aqueous phase by USP type- II (PADDLE) dissolution apparatus. The results of these dissolution studies are listed below in the table. After observing the results, it was found that, nearly 95.55±3.66 % of drug was released from BISMUTH SUBSALICYLATE Pickering emulsion F3 formulation within in 50 minutes compared to other formulations below respectively.

6.4.6 Comparative dissolution studies of different formulations of pickering emulsions

Table 11

Time in minutes	Marketed drug	F1 (0.5%)	F2 (1%)	F3 (1.5%)	F4 (2%)	F5 (2.5%)	F6 (3%)
0	00	00	00	00	00	00	00
5	12.6 ±2.8	18.66±0.92	16.08±0.51	21.11±0.43	19.48±0.62	23.42±0.24	18.59±0.69
10	17.5±2.5	21.12±2.2	21.12±0.77	25.42±0.92	24.28±0.79	26.01±0.01	22.41±0.82
15	21.9±2.5	22.42±3.26	25.33±2.24	30.62±1.24	30.62±0.81	30.24±0.24	25.11±0.05
20	22.6±2.6	26.66±2.24	29.21±0.52	38.42±0.04	36.62±2.24	36.26±1.12	29.52±1.16
25	24.8±2.8	29.22±1.62	31.34±1.52	42.12±1.24	40.43±1.42	39.22±3.42	32.11±0.12
30	26.4± 2.4	30.74±0.09	32.12±0.77	56.41±0.02	51.42±1.24	47.35±0.01	40.62±1.12

35	28..4± 0.8	36.88±2.26	40.22±3.42	64.66±1.2	59.50±0.08	53.42±1.42	46.62±0.02
40	32.8±2.8	46.72±3.42	50.64±2.26	72.42±0.01	68.72±2.42	60.43±2.24	52.62±2.26
45	33.6±3.2	59.22±2.21	56.24±2.23	86.28±1.23	76.24±1.62	66.34±1.67	60.42±1.68
50	36.24±0.18	64.32±1.42	69.72±1.66	90.55±3.66	88.32±2.22	74.12±2.26	76.23±2.22

At the end of the 60 minutes time interval, almost all the drug (90.55±0.01) released from the Pickering emulsion of F3 formulation compared to other drug formulations. Thus, the drug release from the BISMUTH SUBSALICYLATE Pickering emulsion of F3 formulation was found to be significantly higher as compared to that of the other formulations. Hence, this greater availability of dissolved BISMUTH SUBSALICYLATE from the Pickering emulsion of F3 formulation could lead to higher absorption and bioavailability.

7. CONCLUSION

The present study aimed to prepare and evaluate Bismuth subsalicylate Pickering emulsion using PGA Janus particles. Pre-formulation studies were carried out for the drug. Solubility studies were performed using various solvents like DCM, chloroform and Hexa-flouro isopropanol among which Chloroform showed better solubility. Various polymers were tried for the preparation of Janus particles and POLYGLYCOLIC ACID (PGA) showed better solubility with chloroform. The Janus particles were prepared using PGA and chloroform. Six different Pickering emulsion formulations using PGA Janus particles of concentrations like 0.5% , 1% , 1.5% , 2% , 2.5 % and 3 % were prepared. The prepared Pickering emulsions were evaluated for various parameters like viscosity determination, pH determination, conductivity and dissolution studies were performed. From the evaluation studies it was observed that F3 formulation with 1.5% PGA Janus particle concentration was identified as optimized formulation.

From the evaluation tests it is concluded that PGA Janus particleswith 1.5% concentration (F3) can be effectively used for the preparation of Bismuth subsalicylate Pickering emulsion.

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