IOSR Journal Of Pharmacy *www.iosrphr.org*
(e)-ISSN: 2250-3013, (p)-ISSN: 2319-4219
Volume 9, Issue 5 Series. I (May 2019), PP. 66-92

Development and Evaluation of Self Emulsifying Drug Delivery System.

Sachin Poharkar*, Akshay Jannawar,Minakshi Rathod.
Department of Pharmaceutics, Sudhakarrao Naik Institute of Pharmacy, Pusad, Yavatmal 445204 Maharashtra. (India).
Corresponding Author: Sachin Poharkar

Abstract: SDEDDS are poly dispersed systems where the dispersed phase contains the droplets of the continuous phase. These double emulsions are of two types: W/O/W types multiple emulsions and O/W/O types multiple emulsions.
Pantoprazole sodium is a new orally effective proton pump inhibitor agent, highly water soluble drug, is formulated into SDEDDS, which enhances permeability of the drug and produce the sustained release. Liquid SDEDDS formulations were prepared using hydrophilic surfactants Tween80, W/O Emulsion, water and subjected to further evaluation parameter. From the prepared liquid SDEDDS Three optimized Pantoprazole sodium SDEDDS formulations 4:6, 5:5 and 6:4 are selected and evaluated the viscosity and microscopic characterization, high loading drug and emulsification time. With future development of this technology, SDEDDSs will continue to enable novel applications in drug delivery and solve problems associated with the delivery of highly soluble drugs.
There exist some fields of SDEDDS to be further exploited, such as studies about human bioavailability and correlation of in vitro/in vivo. That is, SDE implants/suppositories/microspheres have not been as extensively studied as SDE tablets/pellets/capsules. It is also worth pointing out some issues to which much attention should be paid, for example physical aging phenomenon associated with glyceride, oxidation of vegetable oil , and interactionbetweendrugsandexcipients.Thesedosageformsnotonlyimprovedthebioavailability,drugrelease butalsobyconvertingthemtosolidform,improvedthestabilityandpatientcompliance.Theseformulationsmay further be scaled up for commercialexploitation.

Keyword: microspheres, emulsions, vegetable oil, excipients.

Date of Submission: 25-04-2019 Date of acceptance: 06-05-2019

I. INTRODUCTION

SDEDDS are poly dispersed systems where the dispersed phase contains the droplets of the continuous phase. These double emulsions are of two types: W/O/W types multiple emulsions and O/W/O types multiple emulsions[6].Smallwaterdropletsaredispersedinbiggeroildropletsandtheseoildropletsareagaindispersedin continuous aqueous phases[7], Similarly in O/W/O type multiple emulsions, small oil droplets are dispersed in larger aqueous droplet and these aqueous droplets are again dispersed in continuous oil phase. Their potential pharmaceutical applications include uses such as taste masking, adjuvant vaccines and an immobilization of enzymes, sorbent reservoir of overdose treatments and for enhancement of enteral or dermal absorption[8]. Multiple emulsions have been formulated as cosmetics, such as skin moisturizer. Prolonged release can also be obtained by means of multiplestructures.

These systems have some advantages, such as the protection of the entrapped substances and the incorporation of several actives in the different compartments. Despite their potential usefulness, applications of multiple emulsions have been limited because of thermodynamic instability and their complex structure[9]. The basic rationale for the use of W/O/W and O/W/O type multiple emulsions as means of prolonged delivery of drugs is that the drug contained in the innermost phase of forced to partition itself through several phases prior to release at the absorption site[10]. Thus the partition and diffusion coefficient of the drug and the strength of the middle membrane phase, which is a multi-molecular layer of oil, water, and emulsifier molecules at both the interfaces of multiple emulsion system, control the drug release from these systems[11].Although multiple emulsions are still Infrequently used, their potential applications are numerous and the investigation of these systems is now an active field research, especially in such product areas as pharmaceutical drug delivery systems, cosmetics and foods[12]. Approaches to improve the bioavailability of BCS Class III drugs are:

- Permeationenhancers
- Prodrug

- Chemicalmodification
- Pharmaceuticalmeans
- Multiple / Doubleemulsions

Table no. 1: Biopharmaceutical classification system

PARAMETER	CLASS I	CLASS II	CLASS III	CLASS IV
Aqueous solubility	High	Poor	High	Poor
Permeability	High	High	Poor	Poor
In-vitro in-vivo correlation	Good	Good	Poor	Poor
Absorption rate controlled	Gastric emptying	Dissolution	Permeability	Dissolution & permeability

As per the BCS classification only 34% drugs belong to class I while the remaining 66% drug are class II to IV (17% to class II, 39% to class III and 10% to class IV) [22]. Improving solubility of class II drugs can amplify the concentration of dissolved drug in the GI tract and thus boost the bioavailability.

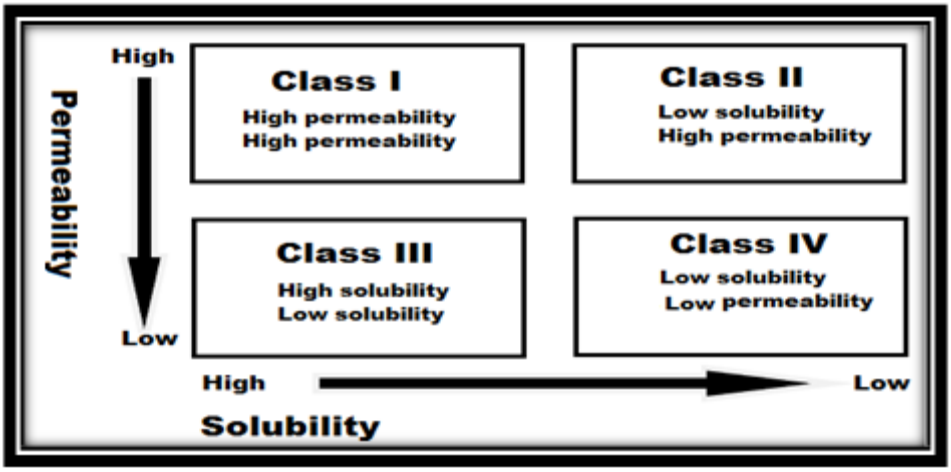


Figure 1: BCS classification of drugs

SEDDS AND SDEDDS:

Water-in-oil-in-water (w/o/w) double emulsions are complex systems consisting of aqueous droplets dispersed within larger oil droplets, which are themselves dispersed in an aqueous continuous phase. The internal aqueous

Dropletsen capsulated by the oil membrane can be see nasa storage chamber for hydrophilic drugs.Thisstructure could protect the drug dissolved in the internal aqueous phase and have shown great promise for enhancing oral bioavailability of low-permeability compounds [4]. Many potential hydrophilic drugs, such as protein andpeptide drugs, administrated orally exhibit low oral bioavailability mainly due to their low intestinal permeability. For this kind of drugs, defined as "high solubility/low permeability class" or biopharmaceutics classification system (BCS) class III, gastrointestinal permeation is the rate-controlling step in the absorption process [2]. Many approaches such as absorption enhancers [3,25], chemical modification [26,27] and pharmaceutical means were used toenhancetheoralbioavailabilityofthosedrugs.Amongtheseapproaches,water-in-oil-in-water(w/o/w)double emulsions show great potential[4,5].

However, the industrial application of double emulsions is limited mainly due to their instability against heat, organic solvents and Ph changes. Although many efforts have been done, no pharmaceutical double emulsions have overcome the research phase and been marketed [28, 29]. Herein, we developed a novel formulation design, self-

doubleemulsifyingdrugdeliverysystem(SDEDDS),whicharetheformulatedmixturesofwater-in-oil(w/o) emulsions and hydrophilic surfactants. Generally, w/o/w double emulsions are prepared by a modified two-step emulsification method. SDEDDS changed the process of the second emulsification step, which canself-emulsify to w/o/w double emulsions due to the gastrointestinal peristaltic movements in vivo instead of artificial emulsificationinvitro.TheconceptofSEDDS wasemployedtorealizethisidea.Self-emulsifyingdrugdelivery systems(SEDDS)areavitaltoolwithgreatpromiseinenhancingtheoralbioavailabilityofpoorlywater-soluble drugs[17,30,31].Asisotropicmixturesofdrug,oilsandsurfactants,thesesystemsrapidlydisperseingastrointestinal

fluidsfollowingtheiroraladministration,yieldingmicro-orNanoemulsionscontainingthesolubilizeddrug [32,33,34].

SimilartoSEDDS,SDEDDScanspontaneouslyemulsifyinthemixedaqueousgastrointestinalenvironment.But the formed emulsions are water-in-oil-in-water (w/o/w) double emulsions not o/w emulsions, and drugs are encapsulated in the internal water phase of the double emulsions. Compared to conventional thermodynamically unstable doubleemulsions,

SDEDDS are stable formulation systems. In addition, SDEDDS can be filled directly into soft or hard gelatin capsule which are easy to administration and storage

COMPOSITION OF SDEDDS:

The self-double emulsifying process is depends on

- Emulsificationequipment
- Nature of the aqueousphase
- Nature of the oilphase
- Volume of dispersedphase
- Nature and quantity of emulsifyingagents
- Added stabilizingcomponent

MECHANISM OF DRUG RELEASE FROM SDEDDS

After formation of double emulsion from SDEDDS, the drug is released from the internal to external phase through the different layer by various mechanisms. The release rates are affected by factors such as droplet size, pH, phase volume and viscosity etc.[50]

Diffusion mechanism

This is the most common transport mechanism where unionized hydrophobic drug diffuses through the oil layer in the stable multiple emulsions. Hence, drug transport follows first order kinetics and obeys Fick's law of diffusion.[51]

Micellar transport

The presence of both lipophilic and hydrophilic surfactants in the oil phase facilitates the formation of water swollen inverse micelle, which acts as carrier for both ionized and unionized drug. Inverse micelles consistingof non-polarpartofsurfactantlyingoutsideandpolarpartinsideencapsulatehydrophilicdrugincoreandpermeate through the oil membrane because of the outer lipophilic nature.[52]

Thinning of the oil membrane

Due to difference in the osmotic pressure, the oil membrane become thin, so the water and drug easily can be diffused. This pressure difference also provides force for the traverse of molecule.[53]

Rupture of oil phase

According to this mechanism, rupturing of oil membrane unites both the aqueous phase and thus drug can be released easily.

Facilitated diffusion (carrier-mediated transport)

This mechanism involves a special molecule (carrier) which combines with drug and makes it compatible to permeatethroughtheoilmembrane.Thesecarrierscanbeincorporatedininternalaqueousphaseoroilmembrane.

Solubilization of internal phase in the oil

Itisaprominenttransportmechanism.Inthis,solubilizationofminuteamountsofinternalphaseinthemembrane phase results in the transport of very small quantities ofmaterials.[54]

PREPARATION OF SDEDDS:

SDEDDS emulsions are best prepared by re-emulsification of primary emulsion. The following are the method of multiple emulsions: 1. Two Steps Emulsification (Double Emulsification) 2. Phase Inversion Technique (One Step Technique) 3. Membrane Emulsification Technique

Two Steps Emulsification (Double Emulsification) [55, 56]:

Two steps emulsification methods involve re-emulsification of primary W/O or O/W emulsion using a suitable

emulsifier agent. The first step involves, obtaining an ordinary W/O or O/W primary emulsion wherein an appropriate emulsifier system is utilized. In the second step, the freshly prepared W/O or O/W primary emulsion isre-emulsifiedwithanexcessofaqueousphaseoroilphase.Thefinallypreparedemulsioncouldbe W/O/Wor O/W/Orespectively.

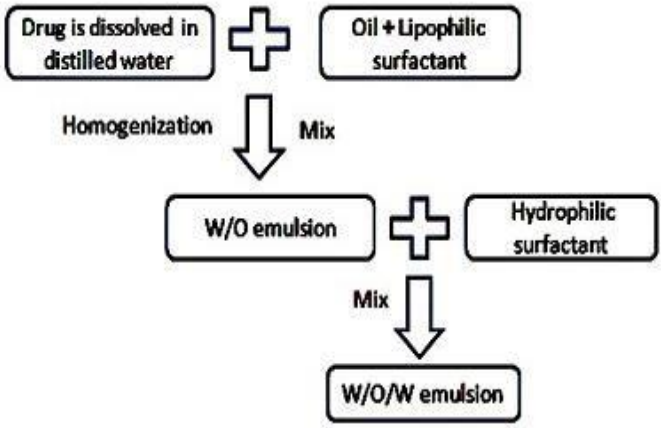


Figure No.2 preparation of SDEDDS

Phase Inversion Technique (One Step Technique)[57,58]

An increase in volume concentration of dispersed phase may cause an increase in the phase volume ratio, which subsequentlyleadstheformationofmultipleemulsions.Themethodtypicallyinvolvestheadditionofanaqueous phase contains the hydrophilic emulsifier [Tween 80/ sodium dodecyl sulphate (SDS) or Cetyl trimethyl ammoniumsaltCTAB)]toanoilphaseconsistedofliquidparaffinandcontaininglipophilicemulsifier(Span80). A well-defined volume of oil phase is placed in a vessel of pin mixer. An aqueous solution of emulsifier is then introduced successively to the oil phase in the vessel at a rate of 5 ml/min, while the pin mixer rotates steadily at 88rpmatroomtemperature.Whenvolumefractionoftheaqueoussolutionofhydrophilicemulsifierexceeds0.7, thecontinuousoilphaseissubstitutedbytheaqueousphasecontaininganumberofthevesicularglobulesamong the simple oil droplets, leading to phase inversion and formation of W/O/W multipleemulsion.

Membrane Emulsification Technique[59]

In this method, a W/O emulsion (a dispersed phase) is extruded into an external aqueous phase (a continuous phase)withaconstantpressurethroughaPorousGlassMembrane,whichshouldhavecontrolledandhomogenous pores. The particle size of the resulting emulsion can be controlled with proper selection of Porous Glass Membrane as the droplet size depends upon the pore size of the droplet size depends upon the pore size of the membrane. The relation between membrane pore size and particle size of W/O/W emulsion exhibits good correlation as described by the followingequation:

Y= 5.03 X + 0.19

Where X is the pore size and Y is the mean particle size of the multiple prepared using membrane emulsifier technique.

FORMULATION APPROACHES :

Differentformulationapproachesthathavebeensoughttoachievesustainedrelease,toincreasethebioavailability and for protection against biodegradation are asfollows:

- **Self-emulsifyingCapsules**
- **Self-emulsifyingTablets**
- **Self-emulsifyingPellets**
- **Self-emulsifyingNanoparticles**
- **Self-emulsifyingBeads**
- **Self-emulsifyingMicrosphere**

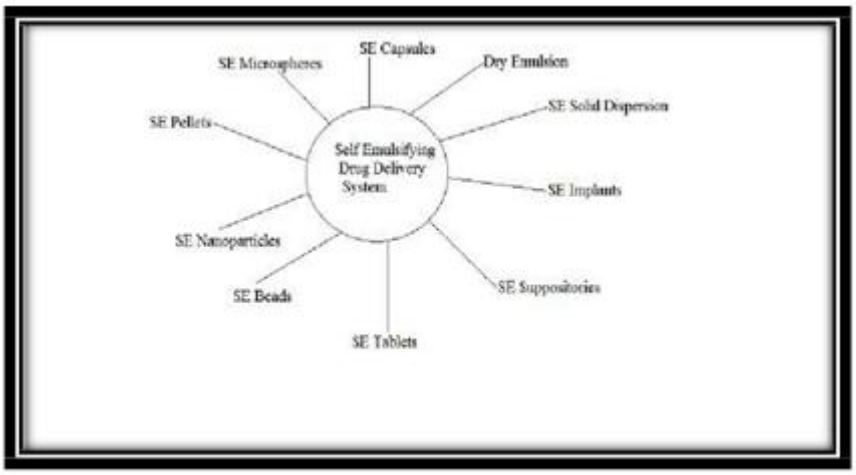


Figure No 3. Types of solid SEDDS

SOLIDIFICATION TECHNIQUES FOR CONVERTING LIQUID /SEMISOLID SEDDS TO S-SEDDS

MELT GRANULATION

Melt granulation is a process in which powder agglomeration is obtained through the addition of a binder that meltsorsoftensatrelativelylowtemperatures.Asaone-stepoperation,meltgranulationoffersseveraladvantages compared with conventional wet granulation, since the liquid addition and the subsequent drying phase are omitted.Awiderangeofsolidandsemisolidlipidscanbeappliedasmeltablebinders.Themainparametersthat control the granulation process are impeller speed, mixing time, binder particle size, and the viscosity of the binder. A wide range of solid and semisolid lipids can be applied as melt able binders. There into, Gelucire1, a family of vehicles derived from the mixtures of mono-/di-/triglycerides and polyethylene glycols (PEG) esters of fattyacids,isabletofurtherincreasethedissolutionratecomparedwithPEGusuallyusedbefore,probablyowing to its SME property.[60] Other lipid-based excipients evaluated for melt granulation to create solid SMES include lecithin, partial glycerides, or polysorbates. The melt granulation process was usually used for adsorbing self-emulsifyingsystem(lipids,surfactantsanddrugs)ontosolidneutralcarriersmainlysilicaandmagnesiumalumina meta silicate [61-63].

ADSORPTION TO SOLID CARRIERS

Free flowing powders may be obtained from liquid self-micro-emulsifying formulations by adsorption to solid carriers. The adsorption process is simple and just involves addition of the liquid formulation onto carriers by mixing in a blender. The resultant powder may then be filled directly into capsule or alternatively, mixed with suitable excipients before compression into tablets. The major advantage of using this technique is good content uniformity. SEDDS can be adsorbed at higher levels (up to 70% w/w) onto suitable carriers. Solid carrier can be microporous substances, high surface area colloidal inorganic adsorbent substances, cross-linked polymers or nanoparticle adsorbent, for example, silica, silicates, magnesium trisilicate, magnesium hydroxide, talcum, cross povidone cross-linked sodium carboxy methyl cellulose and cross linked polymethyl methacrylate. Cross-linked polymers create a favorable environment to sustain drug dissolution and also assist in slowing down drug reprecipitation.Nanoparticleadsorbentscompriseporoussilicondioxide(Sylysia550),carbonnanotubes,carbon Nano horns, fullerene, charcoal and bamboo charcoal.[64-67].

EXTRUSION SPHERONIZATION

The extrusion spheronization process is commonly used in the pharmaceutical industry to make uniformly sized pellets. This process requires the following steps: Mix dry active ingredients and excipients to form a homogeneouspowder;wetmassingwithbinder;extrusionintoaspaghetti-likeextrudate;spheronizationfromthe extrudate to spheroids uniform size; drying; sifting to achieve the desired size distribution. Applying this technique, self-emulsifying pellets of diazepam and progesterone has been prepared to provide a good *in vitro* drug release (100% within 30 min, T50% at 13 min) and bi-layered cohesive self-emulsifying pellets have also been prepared[68-69].

MELT EXTRUSION

Meltextrusionisasolvent-freeprocessthatallowshighdrugloadingapproximately60%.Extrusionisaprocedure ofconvertingarawmaterialwithplasticpropertiesintoaproductofuniformshapeanddensity,byforcingthrough a die under controlled temperature, product flow, and pressure conditions. The size of the extrude aperture will determine the approximate size of the resulting spheroids (Pellets)[70-71].

SPRAY DRYING

This technique involves the preparation of a formulation by mixing lipids, surfactants, drug, solid carriers and solubilizationofthemixturebeforespraydrying.Thesolubilizedliquidformulationisthenatomizedintoaspray of droplets. The droplets are introduced into a drying chamber, where the volatile phase evaporates, and forming dry particles under controlled temperature and airflow conditions. Such particles can be further prepared into tablets or capsules [72-75]. Critical parameters of spray drying includes inlet temperature, outlet temperature, viscosity,solidcontent,surfacetension,feedtemperature,volatilityofsolvent,nozzlematerial.Accordingtothe drying characteristics of the product and powder specification the atomizer, the temperature, the most fitting airflow pattern and the drying chamber design areselected.

7. Experimentalwork:

7.1. Preformulation Studies of Drug[94]

Preformulation can be defined as investigation of physical and chemical properties of drug substance alone and when combined with excipients. Preformulation studies are the first step in the rational development of dosage form of a drug substance. The goals of the program therefore are:

- To establish the necessary physicochemical characteristics of a new drugsubstance.
- To determine its kinetic release rateprofile.
- To establish its compatibility with differentexcipients.

7.1.1 Description

The drug was analyzed for color, odor and taste.

7.1.2 Meltingpoint

Melting point determination of Pantoprazole Sodium was done by open capillary method

7.1.3 Solubility Characteristics

A semi quantitative determination of solubility can be made by adding a solute in small incremental amount to fixed volume of solvents, distilled water, phosphate buffer pH 6.8, buffer pH 1.2, methanol, alcohol, isopropyl alcohol.Aftereachaddition,thesystemisvigorouslyshakenandexaminedusuallyforanyundissolveparticles.

7.2 Spectroscopy

7.2.1 UV-visibleSpectroscopy[95]

7.2.1.1 Determination of λ max

TheUVabsorptionspectrumofPantoprazoleSodiumwasobtainedusingaUV-visibleSpectrophotometer.The spectrumwasscannedfrom200nmto400nm.Atypicalspectrumofpantoprazolesodiumdissolvedindistilled water (Conc. 100µg/ml) is shown in fig4.

7.2.1.2. Standard calibration curve of Pantoprazole Sodium in Phosphate pH 6.8 buffer

i. Preparation of stock solution-

Dissolve 100 mg Pantoprazole Sodium in 100 ml prepared buffer in volumetric flask having conc. 100µg/ml

ii. Preparation of working solution-

Fromstocksolutionpipetteout2,4…20ml.Transferto100mlvolumetricflask&makevolumeupto100with buffertoget2,4…20µg/mlconc.Measuretheabsorbanceat290nmusingUV-visiblespectrophotometer.Plot graph between Conc. vs. Abs. Calculate coefficient of correlation (should between 0.9–1) &slope.

7.2.2 IRSpectroscop

The IR spectrum of drug & excipients was obtained in Aligent technologies cary 630 FT-IRspectrophotometer. FT-IR spectra were recorded in the region of 400–4,000 cm^{-1}. Assign the major absorption bands. Change in absorption bands indicates incompatibility between drug &excipients.

7.3. Solubility studies ofdrug:

Solubility of pantoprazole sodium in various vehicles water, methanol, chloroform, and oils (MCT, oleic acid, soybean oil, sunflower oil), surfactants (Span 80, Tween80) .An excess amount of pantoprazole sodium

(approximately 500 mg) was added to each cap vial containing 5 ml of the vehicles . After sealing stay for 24 hrs. at room temperature ,the samples were centrifuged at 3000×g for 15 min to remove the undissolved pantoprazole sodium. The supernatant was taken and diluted separately with different solvents like acetone , methanol, chloroform for quantification of pantoprazole sodium by uv spectroscopy. Each value represents the mean±SE (n = 3)

7.4. Experimental LIQUID SDEDDS

7.4.1. Preparation of primary emulsion: (dry gummethod):

The primary emulsion is formed from 4 part oil 2 part water and 1 part of emulsifier. 4 part of oil 1part of emulsifier represent the total amount of final emulsion. In a morter 1 part of surfactant levigated with 4 part of oiluntilthepropermixingthenthepantoprazolesodiuminthe2partofwateradded,allatonceandthemixture is vigourously and continually triturated until the primary emulsion formed is creamy white and produce a cracking sound as it is triturated (usually 3-4min.)

7.4.2. Construction of Pseudoternary PhaseDiagrams

Construction of pseudo-ternary phase diagrams Pseudo-ternary phase diagrams were constructed by using the titration method, with the oil phase being replaced by water in-oil (w/o) emulsion. The w/o emulsions was developed by one step emulsification procedure. Pantoprazol sodium was dissolved in distilled water. Then, the PantoprazolsodiumaqueoussolutionwasaddedtotheoilphasewhichconsistedwithMCT,sunfloweroil,Span 80 under moderate magnetic stirring. A series of mixtures that consisted with w/o emulsion and aqueous phase weremadeatcertainweightratios(1:9,2:8,3:7,4:6,5:5,6:4,7:3,8:2,9:1).Eachmixturewasaccuratelyweighedintoglassvialsandmixedhomogeneouslyundermoderatemagneticstirringatroomtemperature.Tween80was then added into each mixture drop-by-drop by a dropper quantitatively. During the titration process, samples were stirred and observed by optical microscopy. At proper concentration of Tween 80, the structure of double emulsions would appear. The concentration of Tween 80 at which double-emulsions formation was obtainedby the weight measurements. These values were then used to determine the boundaries of the double emulsion regions, which is corresponding to the selected optimum ratios of combination vehicles for developing Pantoprazol sodium SDEDDSformulations.

Table 2. Ratio of combination vehicles for developing Pantoprazol sodium SDEDDS formulations:

Sr.No	W/O Emulsion (in ml)	Tween 80 (in ml)
1	1:9	2.7
2	2:8	1.25
3	3:7	0.75
4	4:6	0.50
5	5:5	0.25
6	6:4	0.20
7	7:3	0.15
8	8:2	0.10
9	9:1	0.05

7.5. Method of preparation of self doubleemulsion:

Two methods have been adopted to prepare double emulsions viz: single-step emulsification and two step emulsification processes.

- **Single-step emulsificationprocess:**

Inonestepemulsificationprocess,hydrophilicsurfactantisdissolvedinaqueousphase,hydrophobicemulsifier is incorporated in oil phase and both the phases are subjected to strong mechanical agitation. Water in oil emulsion is formed which is converted to w/o/w doubleemulsion[97].

Besides this, the other method to produce double emulsions is formation of w/o emulsion using hydrophobic surfactant and a little amount of hydrophilic emulsifier with subsequent heat treatment of the formed emulsion till it gets invert. At specific temperature and HLB emulsifiers, w/o/wemulsioncanbeformed.However,theseaccidentalpreparationsarenotreproducible,astheirproduction results in the mutual incidence of catastrophic and transitional inversion of the phases. Hence these systems are referred as transitory or temporary systems. Contrasting the usage of normal small molecule, combination of surfactants is widely used[98].

➢ **Two-stepemulsificationprocess:**Boththehydrophilicandhydrophobicsurfactantsareusedtoproducethe multiple emulsions in this process. Initially, *w/o* type emulsion was developed by one-step technique and then the prepared *w/o* emulsions were added to hydrophilic surfactant (tween 80) under continuous stirring until multiple emulsions are obtained[99]. Pantoprazole sodium having low permeability was formulated as SDEDDS to address the low bioavailability issues along with sunflower oil, span 80, tween 80 . The pantoprazole sodium SDEDDS exhibited goodabsorption.

.

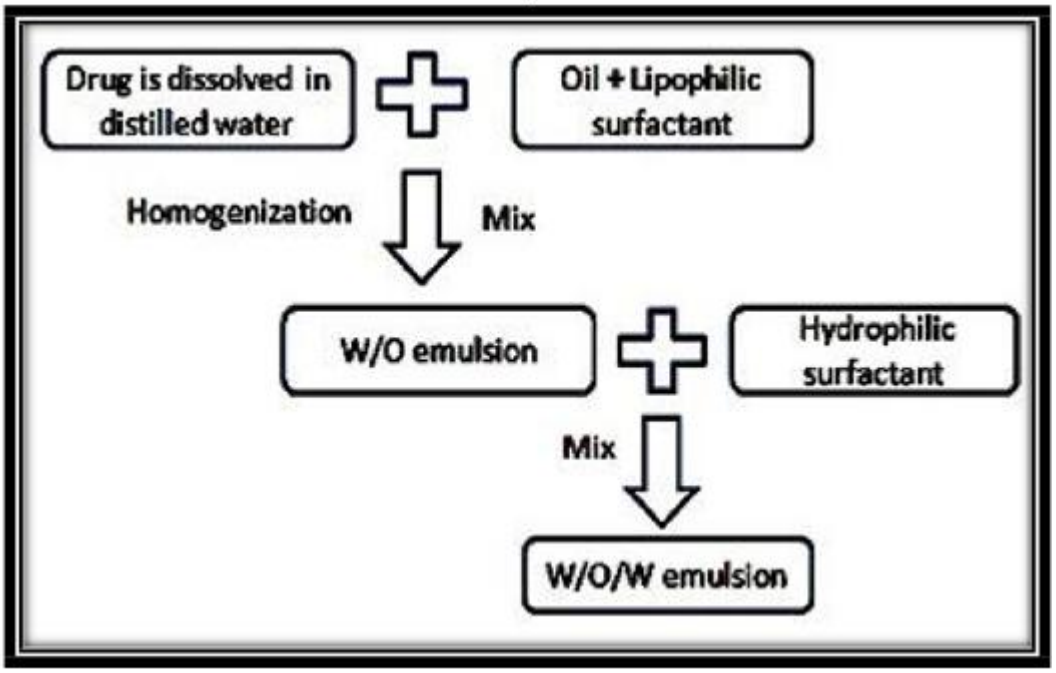


Figure 4: Scheme of double emulsion preparation Table3.Ratio of preparation of self double emulsion

Table3. Ratio of preparation of self double emulsion

Formulation	Ratio	Drug	W/O Emulsion (in ml)	Water (in ml)	Surfactant (in ml)
B1	1:9	2125 mg	4	35.15	10.90
B2	2:8	2000 mg	8.88	35.55	5.33
B3	3:7	1700 mg	13.95	32.55	3.48
B4	4:6	1523 mg	19.04	28.57	2.38
B5	5:5	1950 mg	24.39	24.39	1.19
B6	6:4	2205 mg	29.41	19.60	0.98
B7	7:3	2000 mg	34.48	14.77	0.70
B8	8:2	2000 mg	39.6	9.9	0.49
B9	9:1	2000 mg	44.77	4.97	0.24

7.5.1. Stability Study.

The stability studies were carriedout on these all formulation B1 to B9. The formulation was stored at 40 ± 20^0C/75 ± 5% RH for one month (30 days). After 30 days, samples were withdrawn and evaluated for VISCOSITY, phase sepration, globule size.

Table 4. Stabity study of SDEDDS

Formulation	Ratio	Stability
B1	1:9	Unstable
B2	2:8	Unstable
B3	3:7	Unstable
B4	4:6	Stable
B5	5:5	Stable
B6	6:4	Stable
B7	7:3	Unstable
B8	8:2	Unstable
B9	9:1	Unstable

7.6. PREPARATION OF SOLIDSDEDDS[100-104]

The acceptability of prepared liquid SDEDDS was enhanced by solidification of the liquid SDEDDS into S- SDEDDS by adsorption method. An advantage of the adsorption technique is uniformity of content and high drug loading is possible compared to other techniques. The S-SEDDS offers better stability on long storage and advantages of a solid dosage form (e.g. low production cost, convenience of process control, high stability, reproducibility and better patient compliance).

TheidealsolidAdsorantforpreparationofS-SDEDDSshouldhavehighadsorptioncapacity, whichcouldhold a larger liquid SDEDDS[91] and facilitate the preparation of capsule[28]. From the prepared liquid SDEDDS three formulations 4:6 and 5:5, 6:4 are selected for the preparation of solid SDEDDS based on the percent transmittance and emulsification time. The optimized liquid SDEDDS formulation was transformed into free flowing granules using various porous carriers like Aerosil 200 as adsorbent, which have high surface area, can holdhighamountofliquidonit.).Adsorptionefficiencyofanycarrierisdependentonits porosity,surfacearea and hydrogen bondingcapacity[129]

Aerosil 200 powders were dry and free flowing. The liquid SDEDDS formulation was poured onto the porous carriersplacedinasmallstainlesssteelbowl,mixed,andwetgranulationwasperformedwithhandtoobtainthe homogeneous mass. It was passed through sieve (Sieve No.30) to achieve the uniformly free flowing self emulsifying granules (SEGs). These granules are feel in hard gelatine shell having no"00".

ThePorouscarriersarecharacterizedbystableuniformporousstructures,highsurfaceareas,tunableporesizes withnarrowdistributions,andwell-definedsurfaceproperties,thusallowingthemtoadsorbandreleasethedrugs in a more reproducible and predictable manner. Aerosil 200 has the mean particle size of 12nm.

Table 5: formulation of solid SEDDS

Sr No	Absorbnt	Wt of absorbant	Quantity of liquid SDEDDS
1	Aerosil 200	5 gm	20 ml

EVALUATION OF SDEDDS

Viscosityanalysis

The viscosity of SDEDDS formulation is an important parameter as it relates to emulsion stability and clinical performance.[44]Therheologicalmeasurementsoftheformulationareperformedwithaprogrammablerheometer (Brookfield viscometer). Samples are transferred to the instrument and allowed to equilibrate to 25±1˚C for 10 min prior to the measurement. The apparent viscosity is measured over a shear rate. Viscosities of each formulationaretobemeasuredatdifferentshearratesandthemeanconstantshearviscosityisdeterminedfrom the dataobtained.

Microscopic tests:

The optical microscopy methods are used to analyze and confirm the multiple characters of double emulsions such as type of emulsion, size distribution of droplets etc.

Emulsion droplet size analysis

The droplet size distribution of double emulsions influences the rheology, stability, color and test. These are generally measured by optical microscope using eye piece and stage micrometer. SDEDDS are mixed with distilled water (200 ml) and stirred with mild agitation (75 rpm) on a magnetic stirrer for 5min at room temperature,formingthedoubleemulsions.Theparticlesizedistributionofthedoubleemulsionsisdetermined afterpresentation.Andtheabsorbancevaluesoftheemulsiondropletsarecalculated.Theresultsarereportedas the volume averageMicrometer.[13]

Self -emulsification time

The self-emulsification time is determined by using USP type II dissolution apparatus at 50 rpm, where 0.5gm of SDEDDS formulation is introduced into 250 ml of suitable media (0.1N HCl or 0.5% SLS solution) and the time for emulsification at room temperature is recorded as self-emulsification time for the formulation.[14]

Drug content estimation

Prepared three formulation SDEDDS containing drug equivalent to one dose (10mg) was added in 10 mL volumetric flask containing water and mixed it well. The extracted solution was suitably diluted and analysed for drug content using UV-spectrophotometer at 290 nm.

Micrometrics Properties of pantoprazole sodium S-SDEDDS [109-110]

Determination of Bulk Density, Bulkiness

The bulk density of pantoprazole sodium was determined by the three tap method. 30g of pantoprazole sodium powder was carefully introduced into a 100 ml graduated cylinder. The cylinder was dropped onto a hard wood surface3timesfromaheightof1inchatanintervalof2seconds.Thebulkdensitywasobtainedbydividingthe weightofthesamplebyvolumeofthesamplecontainedinthecylinder.Reciprocalofbulkdensityorthespecific bulk volume gave the bulkiness.

$$\text{Bulk Density} = \frac{\square\square\square\square\square\square\square\square\square\square\square\square(\square\square)}{\square(\square\square^3)}$$

Tapped Density

The tapped density was obtained by dividing the mass of powder by the tapped volume in cm3. The sample of about 30gm of powder is carefully introduced into a 100 ml graduated cylinder. The cylinder was dropped at 2 second intervals onto a hard wood surface 100 times from a height of 1 inch. The tapped density of eachformulation was then obtained by dividing the weight of sample in grams by the final tapped volume in cm3 of the sample contained in the cylinder. It was calculated by using equation given below:
All the estimations were done in triplicate and average are reported in table

Carr's Index

$$\text{Tapped Density} = \frac{\square\square\square\square\square\square\square\square\square\square\square\square(\square\square)}{\square(\square\square^3)}$$

The percent compressibility index (I) of the pantoprazole sodium was calculated using following formula and the results are given in Table 12.

$$\text{Carr's index } \% = \frac{\text{Bulk Density} - \text{Tapped Density}}{\text{Tapped Density}} \times 100$$

Table 6. Relationship between % compressibility & flow ability

% Compressibility	Flowability
5 – 15	Excellent
12 – 16	Good
18 – 21	Fair to Passable
23 – 35	Poor
33 – 38	Very poor
> 40	Extremely Poor

Hausner ratio

Hausner's ratio is an indirect index of ease of powder flow. Lower Hausner's ratio (<1.25) indicates better flow properties than higher ones (>1.25).53 Tapped density and bulk density were measured and the Hausner's ratio was calculated using formula,

$$\text{Hausner's ratio} = \frac{\text{Tapped density (g/cm}^3\text{)}}{\text{Bulk density (g/cm}^3\text{)}}$$

Table 7. Hausner's ratio and compressibility index as an indication of powder flow properties

Sr. No.	Hausner's Ratio	Flow Character	Compressibility Index
1	1.00-1.11	Excellent	<10
2	1.12-1.18	Good	10-15
3	1.19-1.25	Fair	16-20
4	1.26-1.34	Passable	21-25
5	1.35-1.45	Poor	26-31
6	1.46-1.59	Very poor	32-37

Angle of repose

Angle of repose is the angle of inclination, formed to the flat surface by the powder when it is allowed to flow under gravitational force from a fixed height. Samples having angle of repose less than 30°, indicates free flow properties. Angle of repose was measured by fix height funnel method using formula,

$$\theta = \tan^{-1}\left(\frac{h}{r}\right)$$

Where,

θ = angle of repose, h = height of the pile, r = radius of the pile The data presented here is for triplicate determinations.

Table 8. Relationship between angle of repose (θ) and flow ability

Angle of Repose (θ)	Flow ability
< 20	Excellent
20 – 30	Good
30 – 34	Passable
> 40	Very poor

Evaluation of Capsules containing S-SDEDDS Weight variation test for capsules:

20 capsules are taken at random and weighed. Their average weight is calculated, then each capsule is weighed individually and their weight noted. If this requirement is not met, then the weight of the contents for each individual capsule is determined and compared with the average weight of the contents. The contents from the shells can be removed just by emptying or with the help of small brush. From soft gelatin capsules the contents are removed by squeezing the shells which has been carefully cut. The remainder contents are removed by washing with a suitable solvent. After drying the shells, they are weighed and the content weights of the individual capsules are calculated. The requirements are met if [107] not more than 2 of the differences are greater than 10 % of the average net content and [108] in no case the difference is greater than 25 %.

Contentuniformitytest: Thistestisapplicabletoallcapsuleswhicharemeantfororaladministration.Forthis test a sample of the contents is assayed as described in individual monographs and the values calculated which must comply with the prescribedstandards.

In-vitro drug release

The in-vitro dissolution studies are carried out to assess drug release from the formulation.[2] Release profiles fromformulationfilledincapsulesareperformedusingtheUSPtypeIbasketapparatuswith900mlofsuitable dissolution media, 50 RPM at 37±0.5 ◦C. Samples (1 ml) are withdrawn at specified interval of time, filtered using a whatmann filter paper and subsequently analyzed by either UV . Three replicate analyses are carried out for each formulation, and data are used to calculate cumulative drug releaseprofile.

Accelerated Stability Studies[105-106]

In any rationale design and evaluation of dosage forms for drugs, the stability of the active component must be major criteria in determining their acceptance or rejection.The reasons for stability studies are

- There may be chemical degradation of the active drug leading to a substantial lowering the quantity of the therapeutic agent in the dosageform.
- Although chemical degradation of the active drug may not be extensive, a toxic product may be formed in the decompositionprocess.
- Instability of a drug product can lead to a decrease in its bioavailability. This can lead to a substantial lowering in the therapeutic efficiency of the dosageform.

During the stability studies the product is exposed to normal conditions of temperature and humidity. However thestudies willtakealongertime andhenceit wouldbeconvenienttocarryouttheacceleratedstabilitystudies where the product is stored under extreme conditions of temperature. In the present study, stability studieswerecarried out on optimized formulation. The capsules were stored at 40 ± 20 C/75 ± 5 % RH for duration of one

month.AfterintervalofthirtydaysformulationB4,B5andB6waswithdrawnandtestedforphysicalparameter such as drug content and in-vitro drug releasestudies.

Result & Discussion Preformulation Studies Description & melting point

Table 9. Description & melting point of Pantoprazole Sodium

Sr No.	Test	Observation
1	Color	White to off white amorphous
2	Odor	Odorless
3	Taste	Characteristics
4	Melting Point	139–140 ºC

Solubility Characteristics

Table 10. Solubility of Pantoprazole Sodium in different solvents

Sr No	**Solvents**	**Quantity of Dissolved at 25 0 C (mg/ml)**
1	Water	More 1000
2	Methanol	More than 2000
3	Ethanol	More than 1000
4	Acetone	270
5	Chloroform	0.022
6	Dichloromethane	0.018
7	Diethyl Ether	0.001

Aqueous solutions of Pantoprazole Sodium are basic. The pH of a 1.0 % w/v aqueous solution falls in the range of 9.5 to 10.0.Solubility is low at neutral pH & increases with increasing pH.

Spectroscopic Study Determination of λ max

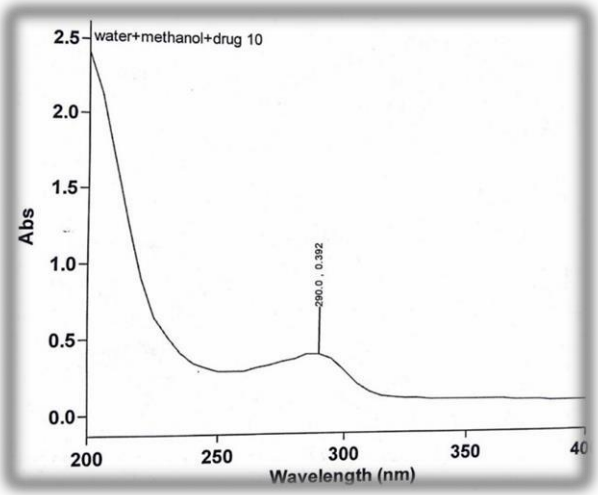


Fig. 5 λ max of Pantoprazole Sodium in water

In Spectroscopic method the maximum absorbance of Pantoprazol Sodium was observed at 290 nm.

Standard calibration curve of Pantoprazole Sodium in water

Table 11.Standard calibration curve of Pantoprazole Sodium in water

Sr No.	Concentration	Absorbance
1	2	0.1145
2	4	0.1790
3	6	0.2652
4	8	0.3526
5	10	0.4373
6	12	0.5389

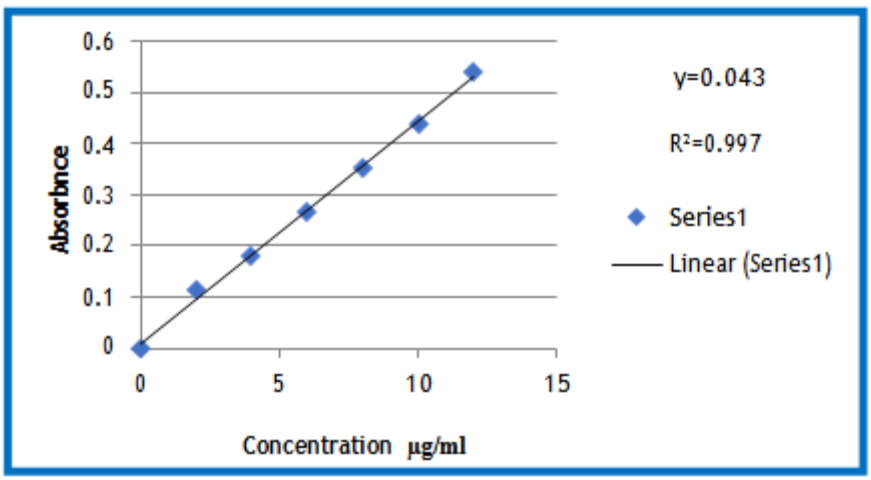


Figure No.6 Calibration curve of Pantoprazole Sodium in water.

Standard calibration curve of Pantoprazole Sodium in Phosphate pH 6.8 buffer

Table 12: Standard calibration curve of Pantoprazole Sodium in Phosphate pH 6.8 buffer

Sr. No.	Concentration (µg/ml)	Mean absorbance at 290nm
0	0	0
1	2	0.0324
2	4	0.0604
3	6	0.0905
4	8	0.1201
5	10	0.1471
6	12	0.1774
7	14	0.2052
8	16	0.2400

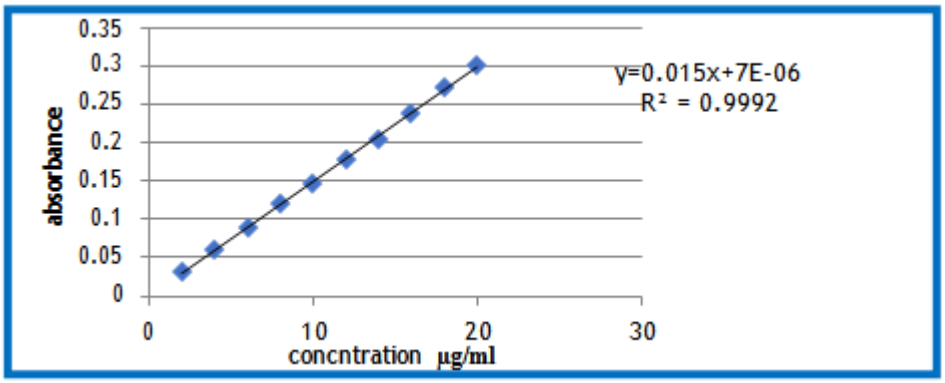


Figure No.7 calibration curve of Pantoprazole Sodium in Phosphate pH 6.8 buffer

Pantoprazole Sodium obeys Beer's Lambert's law in the concentration range of 0–20 µg/ml at 290 nm against pH 1.2 & 6.8 buffer.

Ternary phase diagram;

Pseudo-ternary phase diagram was constructed to identify the self-double- emulsifying regions for the selected vehicle (w/o primary emulsion and Tween 80). As shown in figure area under curve represents the double emulsion region. It is important to determine this area in order to ensure successful conversation of pantoprazole sodium SDEDDS to double emulsion by dilution with distilled water. Combined with surfactant , different ratios of w/o emulsion to surfactant (from 1:9 to 9:1) could spontaneously form water-in-oil-in-water (w/o/w) double emulsions to develop a SDEDDS formulation.

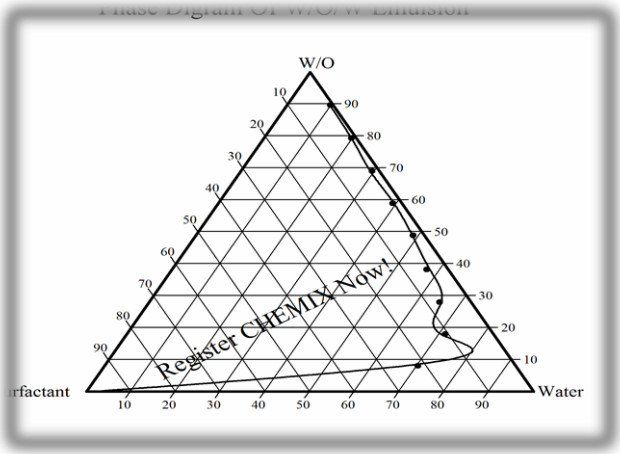


Figure No. 8 Phase Diagram of W/O Emulsion and Surfactant ratio

Selection of optimized batches:

Various ratios of water/ oil emulsion and surfactant are selected and for enhancing the low permeability , the three batches those gives low permeation and that ratio will be suitable for the SDEDDS and enhance the permeability of pantoprazole sodium. From the table no. 7 are selected the three batches i.e B4.B5 and B6 that gives more stability, viscosity and because of this parameters this batches are optimized batch.

IR Spectroscopy

Table No.13 Assignments for the IR absorption bands of drug

Materials	Energy (cm -1)	Assignment
Pantoprazole sodium	3015.83	C–H aromatic stretching
	2944, 2846	C–H aliphatic stretching
	1589	C=N stretching
	1072.47	S=O stretching
	1039.68	CF 2 stretching
	805.32, 1039	C–O of –OCH 3
	822.68	C–C stretching
	805.32 1492.97, 1465, 1451.50, 1428.35	C=C stretching in aromatic ring
	1361.80, 1382.98	C–H bending of CH 2,CH 3

IR spectra of pantoprazole sodium:

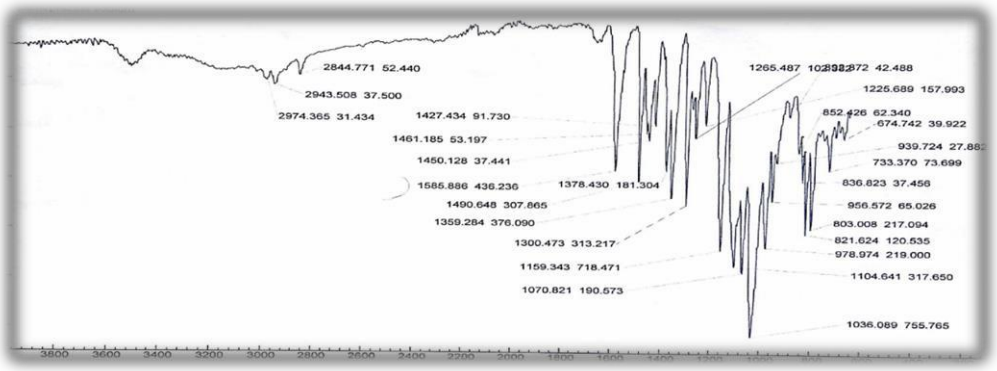


Figure No.9 IR spectra of pantoprazole sodium

Compatibility Studies between Drug and tween 80

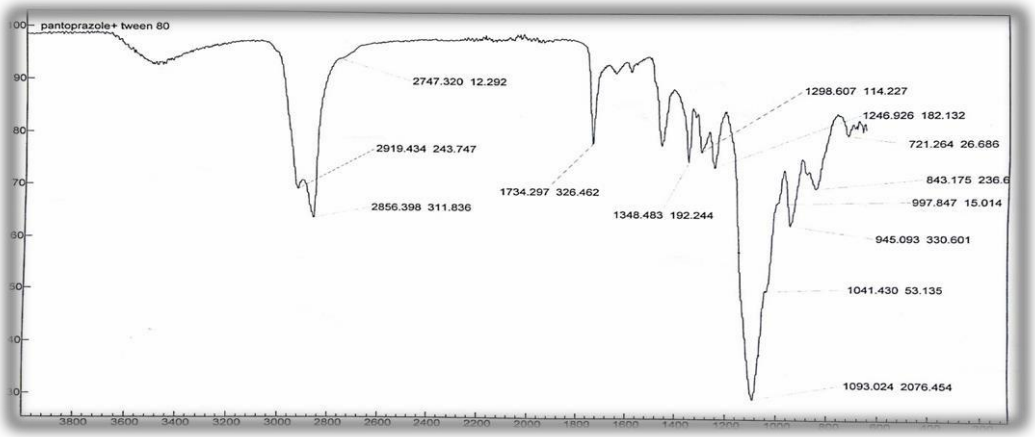


Figure No.10 IR spectra of pantoprazole sodium + tween 80

Compatibility Studies between Drug and spnn 80:

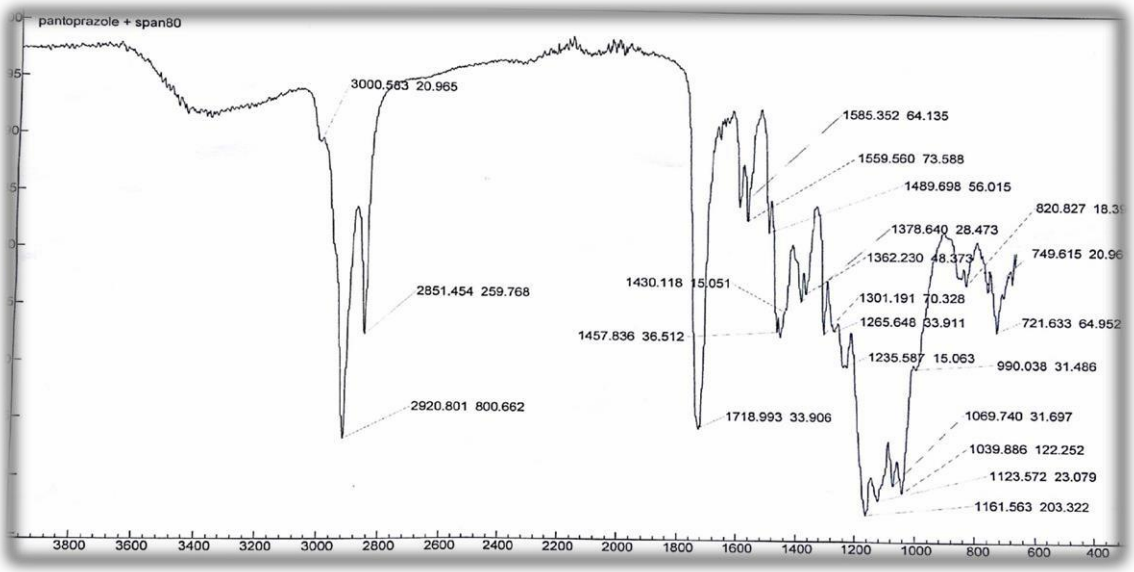


Figure No.11 IR spectra of pantoprazole sodium and span 80

Compatibility Studies between Drug and sunflower oil:

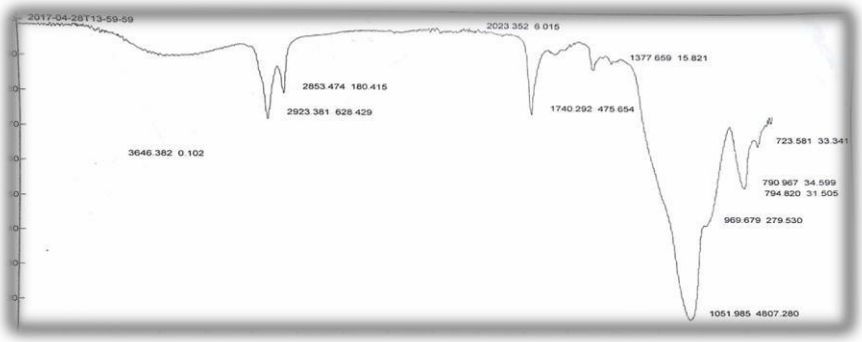


Figure No.12 IR spectra of pantoprazole sodium and sunflower oil

Compatibility Studies of formulation B5

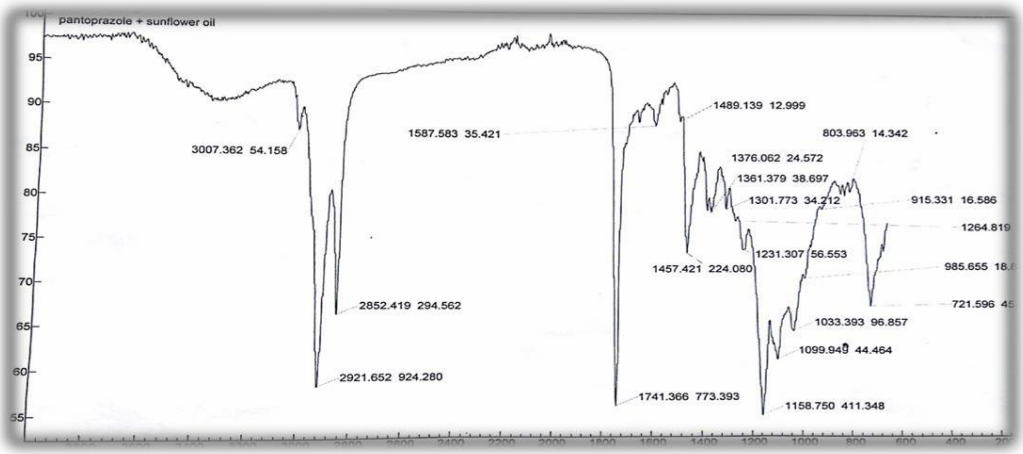


Figure No.13 IR spectra of formulation B5

There was no alteration and no interaction was observed between excipients and drug in combination. All the characteristic peaks of Pantoprazole Sodium were present in combination, thus indicating compatibility between drug and excipients and finally confirm that there was no chemical modification of drug has been taken place.

Solubility of Pantoprazol sodium in different oil, surfactant.

Table .14 Solubility of Pantoprazol in diff. solvent

Sr. No.	Oils	Solubility (mg/ml)
1	Oleic acid	463±0.62
2	Sunflower oil	25.19±0.90
3	Soyabean oil	34.46±0.73
4	Span-80	12.25±1.16
5	Tween-80	23.57±0.54

***All the values are represents as Mean ± S. D. (n=3)**

The comparative solubility studies of the drug in various oils, surfactants are reported in table. 27. As portrayed from the table among the oils Sunflower oil (25.19±0.90mg/mL), among these surfactants tween 80 (23.57±0.54mg/mL),Span-80(12.25±1.16mg/ml)showedlowestsolubilityforPantoprazolSodium.Hence,they were selected for phase titration studies for construction of pseudoternary phasediagrams.

Viscosity of pantoprazol sodium self double emulsion:

The rheological graph states that the flow of viscosity shows non-Newtonian behavior of fluids whose viscosity decreases under shear strain. It is sometimes considered synonymous for pseudoplastic behaviour, and is usually defined as excluding time-dependent effects, such as thixotropy. Thixotropy is a time-dependent shear thinning property. Certain gels or fluids that are thick, or viscous, under static conditions will flow (become thin, less viscous) over time when shaken, agitated, sheared or otherwise stressed (time dependent viscosity).

Table 15. viscosity self-double emulsion

Batch	Viscosity
B 4	182.75
B5	232.25
B 6	280.75

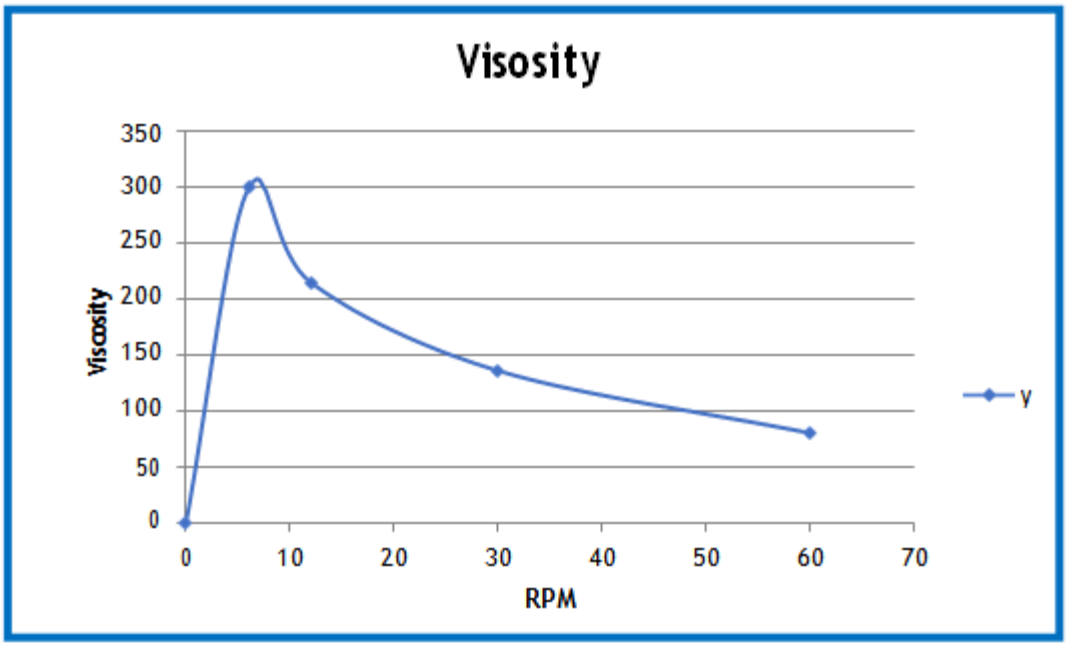


Fig. 14. Viscosity of B4 formulation of SDEDDS

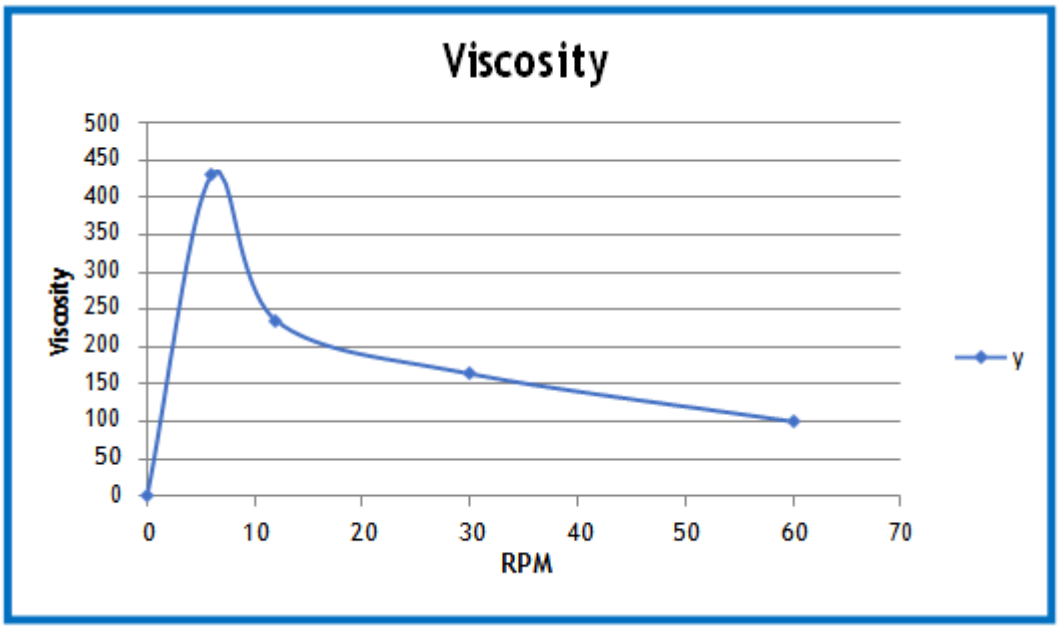


Fig.. 15. Viscosity of B5 formulation of SDEDDS

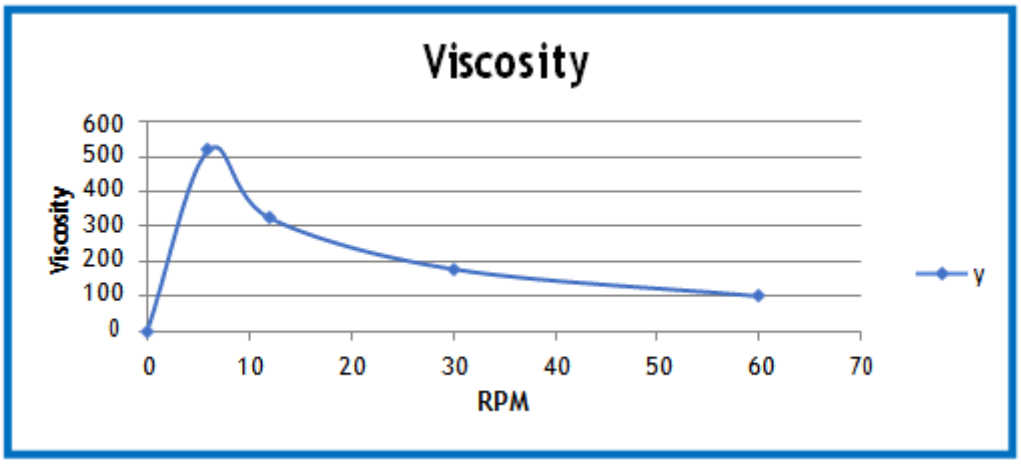


Fig.. 16. Viscosity of B6 formulation of SDEDDS

Emulsification Time

Emulsification time is an important index for the assessment of the efficiency of emulsion formation. SDEDDS should disperse completely and rapidly when subjected to aqueous dilution under mild agitation. Emulsification time of the optimized SDEDDS formulations is shown in Table 20. All the formulations were emulsified within 05 seconds.

Table 16. Emulsification time

Sr. No.	Ratio	Emulsification time (In 0.1 N HCL)
1	6:4 with loaded drug	3 sec
2	5:5 with loaded drug	5sec
3	6:4with loaded drug	4sec

Globule size analysis

The results of globule size of the formulations were found to be 1.530 ± 2.34, 3.491 ± 10.58 and 4.580 ± 3.24 µm respectively. Increase in globule size was result of high drug conc. 44.1 mg/ml in SDEDDS system. The effect of drug incorporation in SDEDDS was found to be influenced by the drug-system physicochemical properties.

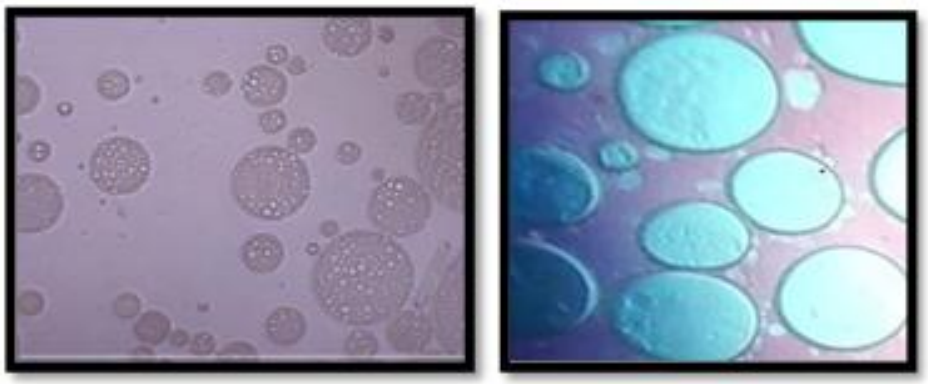


Figure 17: Image of globule size

Micromeritic properties

Table No.17: Micromeritic characterization of prepared Drug Loaded Solid SDEDDS powder.

Formulatio n Batch	Bulk density gm/cm3 mean ± SD	Tapped density gm/cm3 mean ± SD	Carr's index (%) Mean ± SD	Hausner's ratio Mean ± SD	Angle of Repose (0) Mean ± SD
B4	0.5045± 0.0132	0.5789±0.0016	12.85±1.733	1.14±0.025	18.23±0.396
B5	0.4988±0.0051	0.5932±0.0040	15.91±1.03	1.18±0.014	21.45±0.59
B6	0.4678±0.0096	0.5508±0.0035	15.06±1.961	1.17±0.024	21.70±3.063

- **Angle of repose:**

The results of angle of repose of all the formulations were found to be in range of 18.23 ± 0.396 to 21.70 ± 3.63 indicating good flowproperty.
3.64

- **Bulkdensity**:

It has been stated that the bulk density values less than 1.2g/cm^2 indicate good packing and values greater than 1.5g/cm^2 indicate poor packing. The loose bulk density and tapped bulk density values for all the formulation varied in range of 0.4678±0.009g/cm^3 to 0.5045± 0.013g/cm^3 and 0.5508±0.0035g/cm^3 to 0.5932±0.004g/cm^3 respectively. The values obtained lies within the acceptable range.

- **Compressibility index:**

ThepercentcompressibilityofsolidSDEEDSpowderwasdeterminedbyCarr'scompressibilityindex,theresults shown in table no.21. The percent compressibility for all formulation lies within the range of 12.85±1.733% to 15.91±1.03% indicates good flowproperty.

- **Weight variation test:**

In weight variation test, the Pharmacopoeial limit for percent of deviation for capsules weighing from 250mg or moreisnotmorethan10%.Theaveragepercentdeviationofalltabletswasfoundtobewithinthelimitandhence all formulation passes the weight variationtest.

Table 18: Standard physical tests for capsules containing S-SDEDDS

Formulation	Weight variation ± S.D	Drug content (%)
B4	360 ± 0.36	98.76 ± 0.12
B5	329.5 ± 0.29	99.68 ± 0.32
B6	374 ± 0.26	99..21 ± 0.31

* **All the values represent mean ± standard deviation (n=3)**

- **Content uniformity:** The drug content was found to be uniform among all formulation and ranged from 98.76% to99.21%.

In-vitro dissolution study

Table No.19: *In-vitro* dissolution data of B4, B5 and B6 formulation

Time (Hrs)	Cumulative percent drug release		
	B4	B5	B6
0	0	0	0
1	4.07	10.28	17.60
2	8.45	15.75	20.14
3	21.5	18.32	23.78
4	50.57	39.53	31.39
5	55.5	43.60	49.82
6	72.61	55.60	66.85
7	91.42	68.03	76.21
8	93.00	96.21	90.96

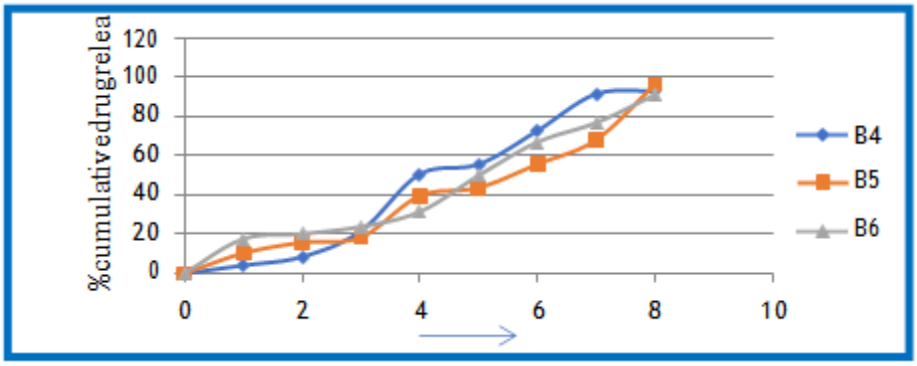


Figure.18: *In-vitro* dissolution profile of B4, B5, B6 formulation

InvitrodrugreleasestudieswereperformedforsolidSDEDDScapsuleB4,B5andB6purePantoprazolesodium powder,usingstandardconditionsinphosphatebufferpH6.8.ItwasobservedthatsolidSDEDDScapsuleofB4, B5andB6showedinprofiledinfigure17.maximumdrugreleasei.e93±0.32,96.21±0.12and90.96±0.40upto 8 hrs. For increase the release rate of drug prepared SSDEDDS.

Accelerated stability study

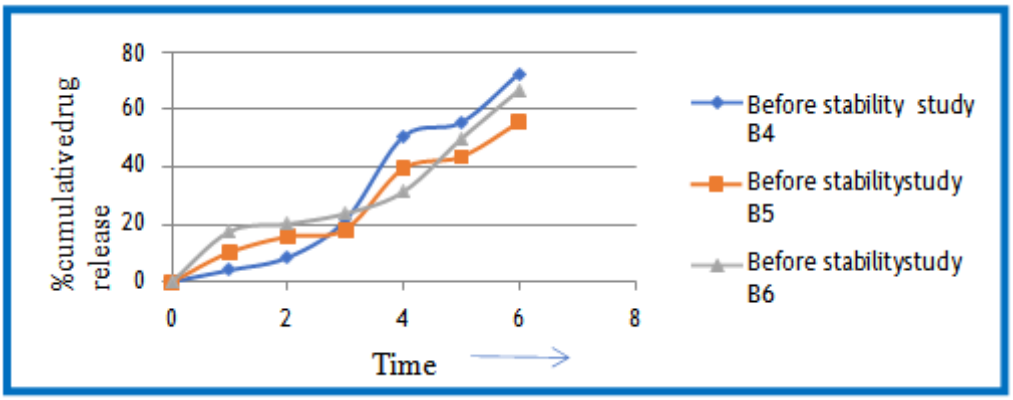
The stability studies were carried out on optimized formulation B4, B5,and B6. The formulation was stored at 40 ± 20^{0}C/75 ± 5% RH for one month (30 days). After 30 days, samples were withdrawn and evaluated for drug content and *in-vitro* drug release studies.

Table No.20: Drug Content Study of B4 , B5 And B6 Formulations Before And After Stability Study

Parameters	Before stability study			After stability study		
	B4	**B5**	**B6**	**B4**	**B5**	**B6**
Drug content	98.76%	99.68%	99.2%	98.70%	99.50%	99.01%

Table No.21: Cumulative percent drug released of optimized formulation B4, B5, B6 before and after stability study

Time (mins)	Before stability study			After stability study		
	B4	**B5**	**B6**	**B4**	**B5**	**B6**
0	0	0	0	0	0	0
1	4.07	10.28	17.60	3.98	10.21	17.56
2	8.45	15.75	20.14	8.40	15.73	20.00
3	21.5	18.32	23.78	20.88	18.29	23.76
4	50.57	39.53	31.39	50.54	39.50	31.34
5	55.5	43.60	49.82	55.34	43.58	49.78
6	72.61	55.60	66.85	72.56	55.57	66.82



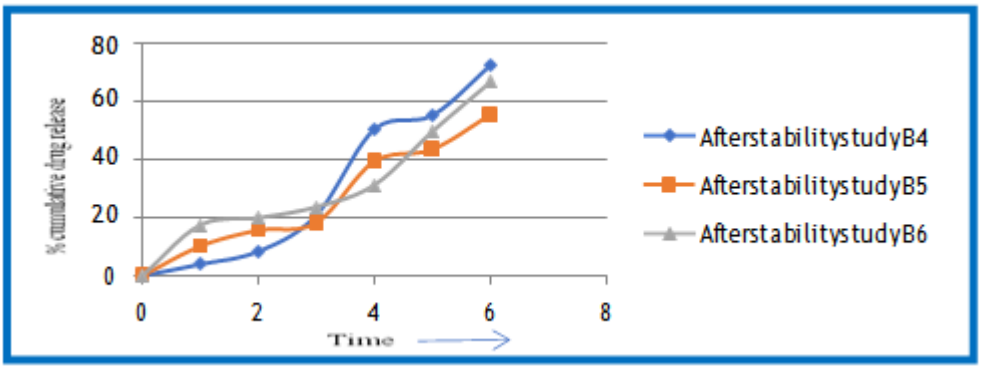


Figure.19 Dissolution profile of formulations B4, B5,B6 before and after stability study

II. SUMMARY AND CONCLUSION

SDEDDS are poly dispersed systems where the dispersed phase contains the droplets of the continuous phase. Thesedoubleemulsionsareoftwotypes:W/O/WtypesmultipleemulsionsandO/W/Otypesmultipleemulsions Self-double emulsifying drug delivery system is a promising approach for the formulation of drug compounds with high aqueous solubility. The oral delivery of hydrophilic drugs can be made possible by SDEDDSs, which have been shown to substantially improve oral bioavailability and its permeability. With future development of this technology, SDEDDSs will continue to enable novel applications in drug delivery and solve problems associated with the delivery of highly solubledrugs.

Thepresentstudyaimstowardsformulationandevaluationofsolidselfdoubleemulsifyingdrugdeliverysyste m such as capsules solid dosage form which can provide sustain release of the modeldrug.

Pantoprazole sodium is a new orally effective proton pump inhibitor agent, highly water soluble drug, is formulated into SDEDDS, which enhances permeability of the drug and produce the sustained release.

The preformulation study of Pantoprazole sodium was performed. The standard curve of Pantoprazole sodium was done in water, methanol & phosphate buffer. The curves show linearity and follows Beer Lamberts law. FT- IR spectrum study reveals that there is no interaction between physical mixture of drug and liquid excipients. λmax of Pantoprazole sodium was found to be 290 nm.

Firstly determine the solubility of pantoprazol sodium in different oils such as oleic acid, soyabean oil and sunfloweroil.Fromthesesolubilityresultsthelesssolubilityofpantopraolsodiuminsunfloweroil,thenprepared primary emulsion of MCT oil such as sunflower oil, lipophyllic surfactant span 80 and water, in absence of drug for construction of psudoternery phasedigram

The pseudoternary phase diagrams were constructed in the absence of drug to identify the region of self double emulsifying and to optimize the conc. of W/O emulsion, water, and surfactant in the SDEDDS formulations by titration method.

Liquid SDEDDS formulations were prepared using hydrophilic surfactants Tween80, W/O Emulsion, water and subjected to further evaluation parameter. From the prepared liquid SDEDDS Three optimized Pantoprazole sodium SDEDDS formulations 4:6, 5:5 and 6:4 are selected and evaluated the viscosity and microscopic chracterisation, high loading drug and emulsification time.

The optimized liquid SDEDDS formulation was transformed into free flowing granules using various porous carriers by adsorption technique like Aerosil 200, as absorbents, which have high surface area, can hold high amount of liquid on it.

From the solid state characterizations of SDEDDS this suggests that Pantoprazole sodium converted from liquid to crystalline state during the preparation of solid SDEDDS using aerosil 200.

FromtheFTIRstudyitisconcludethatthedrugiscompatiblewiththeformulationcomponents.TheS-SDEDDS Granules were evaluated for various parameters. The flow characteristics of the granules were assessed by determining their bulk & tapped density, angle of repose, Hausner's ratio & Carr's Index which were lies within acceptable range. S-SDEEDS powder/granules are feeled in the hard gelti capsules, and further evluated % drug content and *in-vitro* drug releasestudies.

All the formulations comply with the general pharmacopoeial requirement of not more than 10% weight variation. The content uniformity of all formulations found to be in between 98.76 to 99.21%.

In-vitro drug release studies of that Pantoprazole sodium S-SDEDDS capsules B4, B5 & B6 and pure drugwere carried out using USP type I Dissolution Testing Apparatus in 900 ml Phosphate buffer pH6.8

Final formulationB4, B5and B5 were subjected to accelerated stability study. The drug content and dissolution behaviour of prepared formulations remain unchanged during storage.

Hence it can be concluded that solid SDEDDS is a useful technique, to enhance the Permeability and

bioavailability of that Pantoprazole sodium. the different lipophillic emulsifier span 20, span 40, span 60, span 80 on the basis of stability of primary emulsion the span 80 was used. Effect of different hydrophilic emulsifiers tween20,tween40,tween60,tween80ontheperformanceofSDEDDSselecttween80. Thus,thespecificstudy objectives envisaged are achieved, namely formulation, evaluation of self Double emulsifying formulation containing highly water soluble drug for improvement of permeability. These dosage forms not only improved the bioavailability, drug release but also by converting them to solid form, improved the stability and patient compliance. These formulations may further be scaled up for commercial exploitation. Aerosil 200 was showed better granules/powder because of its high specific surface area and oil adsorbing capacity, loading efficiency of SDEDDS.

III. FUTURE SCOPE

Withfuturedevelopmentofthistechnology,SDEDDSswillcontinuetoenablenovelapplicationsindrugdelivery and solve problems associated with the delivery of highly solubledrugs.

Numerous studies have confirmed that SDEDDS substantially improved permeability, absorption and bioavailabilityofhighlywater· solubledrugs.AsimprovementsoralternativesofconventionalliquidSDEDDS, S- SDEDDSaresuperiorinreducingproductioncost,simplifyingindustrialmanufacture,andimprovingstability as well as patient compliance. Most importantly, S- SDEDDS are very flexible to develop various solid dosage formsfororalandparenteraladministration.Moreover,GIinstabilityisavoidable.Thereisstillalongwaytogo, however,beforemoresolidSEdosageformsappearonthemarketbutthereisnomarketedproductofSDEDDS.

Therefore, here is scope to prepare a stable S- SDEDDS and bring it to themarket.

There exist some fields of SDEDDS to be further exploited, such as studies about human bioavailability and correlation of in vitro/in vivo. That is, SDE implants/suppositories/microspheres have not been as extensively studied as SDE tablets/pellets/capsules. It is also worth pointing out some issues to which much attention should be paid, for example physical aging phenomenon associated with glyceride, oxidation of vegetable oil , and interaction between drugs and excipients .

SelectionofsuitableexcipientsisthemainhurdleofdevelopingSSDEDDS.Thus,theseaspectsshouldrepresent the major future working directions for S- SDEDDS. Thus major breakthroughs are still required for proper development ofSDEDDS.

REFERENCES

[1]. YounYS,ImprovedintestinaldeliveryofsalmoncalcitoninbyLys18-aminospecificPEGylation:stability, permeability,pharmacokineticbehaviorandinvivohypocalcemicefficacy,JContr.Release114,2006,334- 342.

[2]. Amidon, G.L., Lennernas, H., Shah, V.P., Crison, J.R., A theoretical basis for a biopharmaceutic drug classification: the correlation of in vitro drug product dissolution and in vivo bioavailability. Pharm. Res.1995, 12,413–420.

[3]. Miyake,M.,Oka,Y.,Minami,T.,Toguchi,H.,Odomi,M.,Ogawara,K.,Higaki,K.,Kimura,T.,Combinatorial use of sodium laurate with taurine or l-glutamine enhances colonic absorption of rebamipide,poorly absorbable antiulcer drug, without any serious histopathological mucosal damages. J. Pharm. Sci2003, 92, 911–921.

[4]. Koga,K.,Takarada,N.,Takada,K.,.Nano-sizedwater-in-oil-in-wateremulsionenhancesintestinalabsorption of calcein, a high solubility and low permeability compound. Eur. J. Pharm. Biopharm. 2010, 74,223–232.

[5]. Shima,M.,Tanaka,M.,Fujii,T.,Egawa,K.,Kimura,Y.,Adachi,S.,Matsuno,R.,Oraladministrationofinsulin included in fine W/O/W emulsions to rats. Food Hydrocolloid 2006,20,523–531.

[6]. HanpramukkunN*.,KongmuangS.,ChansiriG2009.ThestabilityofclindamycinphosphateinW/o/wmultiple emulsions. Int J Pharm Sci Tech 2009 Vol-3, Issue-2, 2009 ISSN:0975-0525.

[7]. oshioka.T, lkeuchi.K, Hashida.M, Murashi. S and sezaki.H, chem. parrm. Bull,1982;30:1408-1410.

[8]. Silva-Cunha, A., Grossiord, J.L., Seiller, M., Multiple Emulsions: Pharmaceutical Potentiality, in: Grossiord JL: Seiller M (eds.), Multiple Emulsions: Structure, Properties and Applications, Editions de Sante, France, 1999, pp 279-312,

[9]. Taelman, M.C., Loll, P., Multiple emulsions in cosmetics. ICI Surfactants, Reprint, RP112/94E,1994.

[10]. Omotosho,J.A.,Whateley,T.L.,Florence,A.T.,Releaseof5-fluorouracilfromintramuscularw/o/wmultiple emulsions.Biopharm. Drug. Disp. 1989, 10:257-268,.

[11]. Ohwaki.T, Nitta.K, Ozawa.H, Kawashimay. Y, Hino.T, Takechu, int. j. Pharm, 1992;85:19-25.

[12]. .Jager-Lezer, N., Denine, R., Grossiord, J.L., Wepierre, J., Rault, S., Seiller, M., Formulating multiple emulsions with moisturizing actives. Cosm. Toilet., 111: 53-58, 1996.

[13]. Lipinski C. Poor aqueous solubility an industry wide problem in drug discovery. Am.Pharm. Rev, 2002: 82- 85.

[14]. Sapra K, Sapra A, Singh SK, Kakkar S. Self Emulsifying Drug Delivery System: A Tool in Solubility Enhancement of Poorly Soluble Drugs. Indo Global Journal of Pharmaceutical Sciences, 2012; 2 (3): 313- 332.
[15]. Padole A, Bodhankar M. Self Double Emulsifying Drug Delivery System (SDEDDS): A Review. Journalof Drug Delivery & Therapeutics, 2012; 2 (6):124-127.
[16]. Brahmankar DM and Jaiswal SB. Biopharmaceutics and Pharmacokinetics-A treatise. 2nd edition., Delhi; VallabhPrakashan: 2010, pp28-29.
[17]. Atef, E., Belmonte, A.A., 2008. Formulation and in vitro and in vivo characterizationof a phenytoin self-emulsifying drug delivery system (SEDDS). Eur. J. Pharm. Sci.35,257–263.
[18]. HanpramukkunN,KongmuangS,etal.Thestabilityofclindamycinphosphateinw/o/wmultipleemulsions. Int J Pharm Sci Tech, 2009; 3 (2):0975-0525.
[19]. Omotosho JA, Whateley TL, et al. Release of 5-fluorouracil from intramuscular w/o/w multiple emulsions. Biopharm. Drug. Disp, 1989; 10:257-268.
[20]. Jager-LezerN,DenineR,etal.Formulatingmultipleemulsionswithmoisturizingactives.Cosm.Toilet,1996; 111:53-58.
[21]. Kumar R, Kumar SM, et al. Multiple Emulsions: A Review. International Journal of Recent Advances in Pharmaceutical Research, 2012; 2 (1):9-19
[22]. Marc L, Sabine K, Dressman JB. Classification of orally administered drugs on the World Health OrganizationModellistofEssentialMedicinesaccordingtothebio-pharmaceuticsclassificationsystem.Eur J PharmBiopharm.2004;58:265-78.
[23]. Brown CK, Chokshi HP, Nickerson B, Reed RA, Rohrs BR, Shah PA. Acceptable analytical practices for dissolution testing of poorly soluble compounds. PharmaTechn.2004:56-65.
[24]. NK Sachan, Biopharmaceutical classification system: A strategic tool for oral drug delivery technology. Asian J Pharma. 2009;3(2):76-81.
[25]. Takatsuka,S.,Morita,T.,Koguchi,A.,Horikiri,Y.,Yamahara,H.,Yoshino,H.,2006.Synergisticabsorption enhancement of salmon calcitonin and reversible mucosal injury by applying a mucolytic agent and a non- ionic surfactant. Int. J. Pharm. 316,124–130.
[26]. Asada, H., Douen, T., Waki, M., Adachi, S., Fujita, T., Yamamoto, A., Muranishi, S., . Absorption characteristics of chemically modified-insulin derivatives with various fatty acids in the small and large intestine. J. Pharm. Sci. 1995, 84,682–687.
[27]. Wang, J., Chow, D., Heiati, H., Shen, W.C., 2003. Reversible lipidization for the oraldelivery of salmon calcitonin. J. Control. Release 88,369–380.
[28]. Benichou, A., Aserin, A., Garti, N., 2004. Double emulsions stabilized with hybrids ofnatural polymers for entrapment and slow release of active matters. Adv. ColloidInterface Sci. 108–109,29–41.
[29]. Benichou, A., Aserin, A., Garti, N., 2007. W/O/W double emulsions stabilized withWPI–polysaccharide complexes. Colloid Surf. A 294,20–32.
[30]. Setthacheewakul, S., Mahattanadul, S., Phadoongsombut, N., Pichayakorn,W., Wiwattanapatapee, R., 2010. Development and evaluation of selfmicroemulsifyingliquid and pellet formulations of curcumin, and absorptionstudies in rats. Eur. J. Pharm.Biopharm..
[31]. Zhao, Y., Wang, C., Chow, A.H., Ren, K., Gong, T., Zhang, Z., Zheng, Y., 2010. Selfnanoemulsifyingdrug deliverysystem(SNEDDS)fororaldeliveryofZedoaryessentialoil:formulationandbioavailabilitystudies. Int. J. Pharm. 383,170–177.
[32]. Gursoy, R.N., Benita, S., 2004. Self-emulsifying drug delivery systems (SEDDS) forimproved oral delivery of lipophilic drugs. Biomed. Pharmacother. 58,173–182.
[33]. Kohli, K., Chopra, S., Dhar, D., Arora, S., Khar, R.K., 2010. Self-emulsifying drug deliverysystems: an approach to enhance oral bioavailability. Drug Discov.Today.
[34]. Singh, B., Bandopadhyay, S., Kapil, R., Singh, R., Katare, O., 2009. Self-emulsifyingdrug delivery systems (SEDDS): formulation development, characterization, and applications. Crit. Rev. Ther. Drug Carrier Syst. 26, 427–521.
[35]. N.S.Barakat. "Enhanced Oral bioavailability of Etodolac by SEDDS: In vitro and in vivo evaluation". J. Pharm. Pharmacol., 2010, 62:173-180.
[36]. M.E.Perlman,S.B.Murdande,M.J.Gumkowski,etal."Developmentofaselfemulsifyingformulationthat reduces the food effects for torcetrapib". Int. J. Pharm.,2008, 351:15-22.
[37]. MannBhupinder1*,RoyGS1,BajwaBS2andKumarSandeep2,"Self-EmulsifiedDrugDeliverySystemfor theEnhancementofOralBioavailabilityofPoorlyWaterSolubleDrugs"IJAPBC–Vol.2(3),Jul-Sep,2013, page no.429-430
[38]. Florence AT, Whitehill D. The formulation and stability of multiple emulsions. Int J Pharm. 1982;11:277.
[39]. Davis SS, Walker IM. Measurement of the yield of multiple emulsion droplets by a fluorescent tracer

technique. Int J Pharm.1983; 17:203-213.
[40]. Garti, N. and Aserin, A. Pharmaceutical emulsion, double emulsion,microemulsion. In microencapsulation
[41]. –Method and Industrial application. Ed. Benita, S. New York, Marcel Dekker: 1996b, 411-534.
[42]. Davis SS, Hadgraft J, Palin KJ. Encyclopedia of Emulsion Technology. Marcel Dekker. New York. 1985; 2:159.
[43]. Davis SS, Walker IM. Multiple Emulsions as Targetable Delivery Systems. Methods in enzymology . 1987; 14,951-64.
[44]. Garti N, Aserin A. Pharmaceutical emulsion, double emulsion, microemulsion. In microencapsulation – Method and Industrial application. Ed. Benita, S. New York, Marcel Dekker: 1996b;411-534.
[45]. Sinha VR and Kumar A. Multiple Emulsion: An Overview of Formulation, Characterization, Stability and Application. Indian. J. Pharm.Sci, 2002; 64 (3):191-199.
[46]. Wakerly MG, Pouton CW, et al. Self emulsification of Veg: oil-Nonionic-Surfactant mixtures. ACS symp. Ser, 1986; 311:242-255.
[47]. DabrosT.Emulsificationthroughareacontraction.JColloidsInterfaceSci,1999;210:222-230.
[48]. Pouton CW. SEDDS: Assessment of the efficiency of emulsion. Int J Pharm, 1985; 27:335-348.
[49]. Reiss H. Entropy induced dispersion of bulk liquids. J Colloids Interface Science, 1975;53:61-70.
[50]. Wakerly MG, Pouton CW, et al. Evaluation of the self emulsifying performance of nonionic surfactant-vegetable oil mixture. J PharmaPharmacol, 1987; 39:6.
[51]. Florence AT, Whitehill D. The formulation and stability of multiple emulsion. Int J Pharm, 1982; 11:277.
[52]. BakerRW,LonsdaleHK.Incontrolledrelease:MechanismandratesControlledreleaseofbiologicallyactive agent. Tonquary AOEEds. Plenum press, New York, 1974;15-40.
[53]. Kita Y, Matsumoto S, et al. An attempt at measuring the stability of w/o/w types multiple phase emulsions by analysing the concentration of ions. Nippon Yaguku Kaishi, 1978; 11:14.
[54]. Madamwar D, Jain N. Photoosmosis through liquid membrane bilayers generated by mixture of bacteriorhodopsis and cyanocobalamine. J Colloid Inter Sci, 1992; 153(1):152-156.
[55]. Khan AY. Potentials of Liquid Membrane System:An overview. Pharmainfo.net, 2007;5(6).
[56]. Dickinson,EandMcClements,D,Water-in-oil-watermultipleemulsion.InAdvancesinFoodColloids.Ed. Dickinson, E and Mc Clements, D. J. Cambridge, UK, Blackie academic and professional:1996,280-300.
[57]. Van der Graaf, S., Schroen, C. and Boom, R. Preparation of Double emulsion by membrane emulsification- a review. Journal of Membrane Science2005,251:7-15.
[58]. Matsumoto, S., Koh, Y. and Michiura, A. Preparation of w/o/w emulsion in an edible form on the basis of phase inversion technique. Journal of Dispersion Science and Technology1985,6(5):507-520.
[59]. Matsumoto, S., and Kang, W. Formation and application of multiple emulsion. JDST, 1989,10(4 & 5):455- 482.
[60]. http://www.scribd.com/doc/24751787/Multiple-Emulsions.
[61]. Porter CH, Trevaskis NL, Charman WN. Lipids and lipid-based formulations: Optimizing the oral delivery of lipophilic drugs. Nature Rev 2007;6:231-248.
[62]. Amit Kumar Nayak , Sougata Jana, "A Solid Self-Emulsifying System for Dissolution Enhancement of Etoricoxib" Journal of PharmaSciTech 2013;2(2):87-90
[63]. SeoA,HolmP,KristensenH.G,SchæferT,Thepreparationofagglomeratescontainingsoliddispersionsof diazepam by melt agglomeration in a high shear mixer, Int J Pharm, 2003, 259, 161-171.
[64]. Gupta M K, Goldman D, Bogner R H, Tseng Y C, Enhanced drug dissolution and bulk properties of solid dispersions granulated with a surface adsorbent, Pharm Dev Technol. 2001, 6,563-572
[65]. Lijuan Wang, Jinfeng Dong, Design and Optimization of a new self nano emulsifying drug delivery system, Journal of colloid and interface science 2008;1-6.
[66]. Ito Y, Kusawake T, Ishida M, Oral solid gentamicin preparation using emulsifier and adsorbent, J Control Release, 2005, 105, 23-31.
[67]. Venkatesan N, Yoshimitsu J, Ito Y, Shibata N, Takada K, Liquid filled nanoparticles as a drug delivery tool for protein therapeutics. Biomaterials 2005, 26,7154-7163.
[68]. FuldenBuyukozturkandHongLong.Selfemulsifyingdrugdeliverysystemreleasekinetics.Dependenceon physical and chemical emulsion formulation properties. Nanosystems for drug delivery.2007;18(2):25-27.
[69]. Iosio T et al, Bi-layered self-emulsifying pellets prepared by co-extrusion and spheronization: influence of formulation variables and preliminary study on the in vivo absorption, Eur J Pharm Biopharm, 2008, 69(2), 686-697.
[70]. Newton M, Petersson J, Podczeck F, Clarke A, Booth S, The influence of formulation variables on the properties of pellets containing a selfemulsifying mixture, J Pharm Sci, 2001, 90,987-995.
[71]. Newton J M et al, Formulation variables on pellets containing self-emulsifying systems, Pharm Tech Eur, 2005, 17,29-33.

[72]. TaoYi.,JianglingWan.Anewsolidself-microemulsifyingformulationpreparedbyspray-dryingtoimprove the oral bioavailability of poorly water soluble drugs. Eur. J.Pharm. andBiopharm. 2008;70:439-444.
[73]. Verreck G, Brewster M E, Melt extrusionbased dosage forms, excipients and processing conditions for pharmaceutical formulations, Bull Tech Gattefosse, 2004, 97,85-95
[74]. WeiWu.,YungwangLiQue.Enhancedbioavailabilityofsilymarinbyself-microemulsifyingdrugdelivery system. Eur.J.Pharm and Biopharm. 2006;63:288-294.
[75]. MadhavVasanthavada., Abu T M Serajuddin. Lipid based selfemulsifying solid dispersions. Drugs and the Pharmaceutical sciences.2006; 170:149-182.
[76]. Shafiq. Development and bioavailability assessment of ramiprilnanoemulsion formulation. Eur. J. Pharm. Biopharm 2007;66:227-243.
[77]. Xiaona Wang, Sifan Jiang, Xinyue Wang, Jie Liao, ZongningYinPreparation and evaluation of nattokinaseloadedself-double-emulsifying drug delivery system asian journal of pharmaceutical sciences 10 2015.386–395.
[78]. Xiaole Qi, Lishuang Wang, Jiabi Zhu, Zhenyi Hu, JieZhangSelf-double-emulsifying drug delivery system (SDEDDS): A new way for oraldelivery of drugs with high solubility and low permeability International Journal of Pharmaceutics 409 (2011)245–251.
[79]. PrasannaRaju Y1*, Gowri Y2, HariniChowdary V3, BasaveswaraRao MV3, Sundaresan CR4Contemporary StrategiesinEmulsifiedDrugDeliverySystems:ARetrospectiveOverviewJordanJournalofPharmaceutical Sciences, Volume 10, No. 1,2017
[80]. Sachin M. Kolhe1., Arun T. Patil2., Pradeep P. Bawane1., Jineetkumar B. Gawadl,Development and Evaluation of Solid Self Double Emulsifying Drug Delivery System(SSDEDDS) : A Novel Approach to Enhance Bioavailability of BCS Class III Drugs,Journal of Pharmacy Research2016,10(6),403-409.
[81]. Li Zhang, Quan Zhang, Peng Zhou, Gong Tao, Zhirong Zhong, Zhirong Zhang, Enhanced absorption of Stachydrine using a self-double-emulsifying drug delivery systems (SDEDDS): invitro and in vivo studies, Life Science Journal2013;10(4).
[82]. VisheshKumarPal,selfemulsifyingdrugdeliverysystems,JournalofPharmaceuticalResearchAndOpinion 1:3 (2011) 80 – 84.
[83]. Xiaole Qi a,1, Jiayi Qin a,1, Ning Maa, Xiaohua Chou a, Zhenghong Wua,b,* Solid self-microemulsifying dispersible tablets of celastrol: Formulation development, charaterization and bioavailability evaluation "International Journal of Pharmaceutics 472 (2014)40–47
[84]. Komal Jayshankar Chourasia and Nilesh Mahadeo Khutle, self double emulsifying drug delivery system: a Comprehensive review, world journal of pharmacy and pharmaceutical sciences Volume 4, 2015,433-447.
[85]. Smita S. Pimple, Swapnil E.Yeole, Pravin D. Chaudhari. "Formulation and Evaluation of Self Micro EmulsifyingDrugDeliverySystemforPoorlyWaterSolubleDrugRisperidone"Int.J.Pharm.Sci.Rev.Res., 23(1),Nov–Dec2013;n°31,155-162.
[86]. KavitaSapraa,AshuSaprab,SKSingha,SaloniKakkarb,SelfEmulsifyingDrugDeliverySystem:ATool in Solubility Enhancement of Poorly Soluble Drugs, ndo Global Journal of Pharmaceutical Sciences, 2012; 2(3):313-332
[87]. ShilpiRawat ,Derle , Parve and Shinde . Self emulsifying drug delivery system (sedds): a method for bioavailability enhancement, IJPCBS 2014, 4(3),479-494
[88]. Anna Czajkowska-Ko´snik 1,, Marta Szekalska 1, Aleksandra Amelian , Emilia Szyma´ nska And katarzynawinnicka 1, Development and Evaluation of Liquid and Solid Self-Emulsifying Drug Delivery Systems ForAtorvastatin
[89]. Europeanpharmacopoeia
[90]. The United States Pharmacopeial Convention Revision Bulletin Official October 1,2010
[91]. Polysorbate 80 Wikipedia, the free encyclopedia
[92]. www.Aerosil.com
[93]. Durgacharan arun bhagwat, john intru d'souza, formulation and evaluation of solid self micro emulsifying drug delivery system using aerosil 200 as solid carrier, bhagwat and d'souza, international current pharmaceutical journal 2012, 1(12):414-419.
[94]. Adnan A. Badwan et al., Analytical Profiles of Drug Substances & Excipients, Vol 29, Edited by Harry G. Brittain, Academic Press,213–259.
[95]. LachmanL,LiebermanHA,KanigJL,TheTheoryandPracticeofIndustrialPharmacy,VarghesePublishing House Bombay, 2nd Ed.,171–196.
[96]. Government of India Ministry of Health & Family Welfare, Indian Pharmacopoeia 2010, Published by The India Pharmacopoeia Commission,Ghaziabad,VolI,559–560.
[97]. RaymondCRowe,PaulJSheskeyandsiancowenhandbookofpharmaceuticalexcipientsfifthedition760- 761

[98]. Garti,N.andAserin,A.Doubleemulsionsstabilizedbymacromolecularsurfactants.*Adv.Colloid.Interface Sci.,* (1996); 65:37-69.
[99]. Hong, L., Sun, G., Cai, J. and Ngai, T. One step formation of *w/o/w* multiple emulsions stabilized by single amphiphilic block copolymers. *Langmuir*, (2012); 28 (5):2332-2336.
[100]. Qi, X., Wang, L., Zhu, J., Hu, Z. and Zhang, J. Selfdouble-emulsifying drug delivery system (SDEDDS): A new way for oral delivery of drugs with high solubility and low permeability. *Int. J. Pharm.*, (2011); 409: 245
[101]. Sarwar Beg, Suryakanta Swain, Harendra Pratap Singh, Ch Niranjan Patra, and ME Bhanoji Rao, Development, Optimization, and Characterization of Solid SelfNanoemulsifying Drug Delivery Systems of Valsartan Using PorousCarriers.

[102]. Bhagwat DA, D'Souza JI. Formulation and evaluation of solid self micro emulsifying drug delivery system using aerosil 200 as solid carrier. Int Curr Pharma J.2012;1(12):414-9.
[103]. Kyatanwar AU, Gajbhiye ND, Jadhav KR, Kadam VJ. Solid self emulsifying drug delivery systems: A review. J Pharmacy Res. 2010 ;3(4):877-82.
[104]. Milovic M, Djuris J, Djekic L, Vasiljevic D, Ibri S. Characterization and evaluation of solid self-microemulsifyingdrugdeliverysystemswithporouscarriersassystemsforimprovedcarbamazepinerelease. Int J Pharm. 2012;436:58-65.
[105]. Sher P, Ingavle G, Ponrathnam S, Pawar AP. Low density porous carrier based conceptual drug delivery system. Mesoporous Materials. 2007; 102:290-98.
[106]. KanvindeSA,KulkarniMS.,Stabilityoforalsoliddosageforms–Aglobalperspective,*PharmaTimes*,2005; 37(5):9-16.
[107]. www.ICH/stability.
[108]. Pharmaceutics – The Science of Dosage form Design by M.E. Aulton, 2nd Edition. 108.Remington – The Science and Practice of Pharmacy, 20th Edition, Volume –1.
[109]. Aulton ME., The Science of dosage form design; Churchill living stone; 2nd ed; 2002;414-418.
[110]. MartinA.,PhysicalPharmacy,PhysicalChemicalPrinciplesinthePharmaceuticalSciences,thirdedition,
[111]. B.I. Waverly Pvt. Ltd, New Delhi.

IOSR Journal of Pharmacy (IOSR-PHR) is UGC approved Journal with Sl. No. 3365, Journal No-62875

Sachin Poharkar. "Development and Evaluation of Self Emulsifying Drug Delivery System..". IOSR Journal of Pharmacy (IOSRPHR), vol. 9, no. 5, 2019, pp. 66-92.