Review Article **CODEN: IJRPJK** **ISSN: 2319 – 9563**

International Journal of Research in Pharmaceutical and Nano Sciences

Journal homepage: www.ijrpns.com

https://doi.org/10.36673/IJRPNS.2021.v10.i05.A35

FORMULATION AND CHARACTERISATION OF EMULSION

Mahitha[*1], A. P. Chaithanya[1], T. K. Ajith Babu[1]

[1*]Malik Deenar College of Pharmacy, Seethangoli, Bela, Kerala 671321, India.

ABSTRACT

The proper style and formulation of a indefinite quantity form needs thought of the physical, chemical and biological characteristics of all of the drug substances and pharmaceutical ingredients to be utilized in fabricating the merchandise. The drug and pharmaceutical materials used should be compatible with each other to provide a drug product that's stable, efficacious, attractive, simple to administer and safe. The merchandise ought to be factory-made below applicable measures of internal control and packaged in containers that contribute to product stability. The merchandise ought to be tagged to push correct use and be hold on below conditions that contribute to most period. Ways for the preparation of specific styles of indefinite quantity forms and drug delivery systems area unit delineated in resulting chapters. This chapter presents some general issues concerning pharmaceutical Ingredients, drug product formulation, and standards permanently producing apply of emulsion.

KEYWORDS

Emulsion, Stability, Evaluation and Pre-formulation.

Author for Correspondence:

Mahitha,

Malik Deenar College of Pharmacy,

Seethangoli, Bela, Kerala 671321, India.

Email: mahithahari1999@gmail.com

INTRODUCTION

An Emulsion is a mixture of two or more liquids that are normally immiscible (unmixable) owing to liquid-liquid phase dispersion. Emulsions are the part of a more general class of two phase systems of matter which is called as colloids. Emulsion should be used when both phases i.e. dispersed and continuous phases are liquids. An emulsion is a thermodynamically unstable system in which one liquid (the dispersed phase) is dispersed as globules in the other liquid (the continuous phase).

Examples of emulsions include, homogenized milk, liquid bimolecular condensates and, cutting fluids which is used in metal purposes.

Different types of emulsions can be formed with two liquids.

Example, oil and water can form,

Simple emulsion

An oil-in-water emulsion, in which the oil is the dispersed phase, and water is the continuous phase. In a water-in-oil emulsion, where water is the dispersed phase and oil is the continuous phase.

Multiple emulsions

Multiple emulsions are also possible to form which includes a "water-in-oil-in-water" (w/o/w) emulsion and an "oil- in-water-in-oil" (o/w/o) emulsion.

Micro emulsion

Clear transparent solutions, particle size ranges from 10-200nm.

Emulsions, being liquids, do not exhibit a static internal structure.

Advantages

Mask the unpleasant taste.

Sustained release medication.

Inert and chemically non – reactive.

Reasonably odourless and cost effective.

Disadvantages

Thermodynamically unstable and have short shelf-life

Leads to creaming and cracking and to phase inversion[1,2].

GMP REQUIREMENTS OF EMULSION

A good manufacturing practice is a system which is used for ensuring that products are consistently produced and controlled according to quality standards. It is also designed accordingly to minimize the risks involved in any pharmaceutical production that cannot be eliminated through testing the final product. Good manufacturing practices is a regulation of government manufacturing of days of consistent quality, purity and efficacy provided under schedule M of Drugs and Cosmetics

Rule 1945 components of GMP include,

Buildings and facilities

Equipment

Raw materials

Premises

Manufacturing of sterile products

Complaints

Sanitization

Records

Sterile products finishing of sterile products

Buildings and facilities

The designs of facilities are largely dependent upon the types of products manufactured and potential for cross contamination and microbiological contamination equipment.

There must be appropriate facilities in the production area with proper supply of good quality of water

Equipment

Equipment should be of sanitary design. This includes sanitary pumps, valves, flow meter which can be easily sanitized.

Raw material

The physical characteristics particularly the particles size of drug substances are very important for emulsion.

Manufacturing of sterile products

Should have provisions for separate extended area specially designed for sterile product. Manufacturing area must be airlock entry with restricted entry.

Manufacturing area should be with adequate space and arranged to prevent cross contamination.

Quality control

Quality control is important step in the manufacturing of the drug substance includes - The testing of bulk components, testing of finished products prior to sale, stability programmes.

Finished products offer packaging should be stored in the finished goods store within an area marked and subjected to quality control test.

Records

Documentation of all the GMP activities. Record must be readily available.

The comfort of the personnel working and regular monitoring of temperature and humidity, particles count etc.

SPECIFIC REQUIREMENTS FOR THE MANUFACTURE OF EMULSION
{PART 1-C}

Buildings and equipment

The premises and equipment's shall be designs, constructs and maintains to suit the manufacturing of emulsions.

The layout and the design can minimize the risk of cross-contamination and mix-ups.

The manufacturing area shall have entry through double door air lock facility.

Drainage shall be of adequate size and have adequate traps, without open channels and design shall be shallow to facilitate cleaning and disinfecting.

The production area shall be sanitized and cleaned at the end of every production process.

Tanks, containers, pipe works and pumps shall be used designed and installed so that they can be easily cleaned and sanitized.

Equipments design shall be such as to prevent the accumulation of residual microbial growth or cross contamination.

The arrangement for cleaning of containers, closures and droppers shall be made with the high pressure air, water, and steam jets.

The furniture shall be smooth, washable and made of stainless steel.

Purified water

The chemical and microbiological quality of purified water used shall be specified and monitored routinely.

The microbiological evaluation shall include testing for absence of pathogens and shall not exceed 100cfu/ml.

There shall be a written procedure for operation (SOP) and maintenance of the purified water system.

Care shall be taken to avoid the risk of microbial contamination with certain methods like re-circulation, use if UV treatment, with heat and sanitization agents after treatment with a chemical sanitization agent, a flushing shall be done to ensure that the sanitizing agent has been effectively removed.

Manufacturing

Manufacturing personnel shall wear non-fibre shedding clothing to prevent contamination of the product.

Certain materials such as gunny bags, wooden pallets etc. can't be carried into the area where products or cleaned containers are exposed.

Care must be taken to maintain the homogenicity of emulsion by use of appropriate emulsifier .Mixing and filling process shall be specified and monitored.

Special care should be taken at the beginning of the filling process and at the end of the process to ensure that the product is uniformly homogenous during the filling process.

The maximum period of storage time of the product on bulk stage shall be validated[3].

PREFORMULATION

Preformulation studies should focus on those physicochemical properties of the new compound that could affect drug performance and development of an efficacious dosage form. Preformulation could also be delineated as a stage of development method throughout that the researches characterize the physical, chemical, and mechanical properties of the drug substance to from effective, stable and safe indefinite quantity type thus, Preformulation studies are essential to characterize the drug for correct coming up with of the drug delivery system. The Preformulation studies which were performing in this include,

Description

The drug powder was examined for its organoleptic properties like colour, taste and odour.

Melting point

The temperature was firm by the capillary technique mistreatment Digital temperature equipment. Once the drug was packed into all-time low of the tube, the tube was placed into the slot of the equipment, the equipment was started and therefore the temperature was noted at that the drug soften. The capillary was consolidated and stuffed by pressing the open finish gently into pure drug sample and packed by sound all-time low of the capillary on a

tough surface so the drug packed down into all-time low of the tube.

Solubility studies

The sample was qualitatively tested for its solubility in numerous solvents. it had been determined by taking ten mg of drug sample in ten cubic centimetre of solvent as water, methanol, ethanol, acetonitrile, pH scale buffer half dozen. 8 in little take a look at tubes and well solubilized by shaking.

Hygroscopic Nature

Identification of drug sample

Drug- excipients compatibility studies

PREFORMULATION PARAMETERS

Solubility – aqueous solubility, intrinsic solubility

PKa from solubility data

Solvents

Partition coefficient

Stability study – creaming and coalescence

Solubility

Solubility is outlined because the most quantity of a substance that may dissolve in a very given quantity of solvent at a nominative temperature. Liquid solubility is that the concentration of the chemical within the liquid part, once the answer is in. Intrinsic solubility of a compound is that the concentration in equilibrium with the solid half that dissolved into the solution. Equilibrium with the pure compound in its usual half (gas, liquid or solid) at a nominative temperature and pressure.

PKa from solubility knowledge

At constant ionic strength the pH-dependent solubility of Associate in Nursing ionogenic compound will be calculated by means that of a technique delineate by Hans Adolf Krebs and Speakman (Krebs, Speakman, 1945) if the pKa worth of the substance and also the solubility of the neutral molecular kind are famed.

Solvents

Solvents could also be preponderantly acidic, preponderantly basic, amphoteric (both), or aprotic (neither). Polar solvents (e.g., water) favour formation of ions; non polar ones (e.g., hydrocarbons) do not. Solvent substance, commonly a liquid, among that various materials dissolve to form a solution.

Partition constant

Partition coefficients are outlined because the concentration magnitude relation of a chemical between 2 media at equilibrium. Partition coefficients will be measured by experimentation in varied ways that (by shake-flask, HPLC etc.) or calculable by calculation supported a range of strategies (fragment-based, atom-based, etc.).

FORMULA

$$\text{Partition coefficient(p)} = \frac{\text{conc. of Drug in org. phase.}}{\text{conc. of Drug in aq. Phase.}}$$

Stability study

Union of emulsions is Associate in Nursing process by that 2 or additional drops merge throughout contact to create one female offspring droplet. The increase of form to the surface of Associate in Nursing emulsion is cited as creaming, that happens because of density variations between the {dispersed particles|dispersed phase|} and also the body fluid phase[4].

CRITERIA FOR EXCIPIENT SELECTION

Excipients are substances apart from the active pharmaceutical ingredient that are fittingly evaluated for safety and are by design enclosed in a very drug delivery system.

Ideal properties of an excipeint

No interaction with drug

Physical and chemical stability

Non nephrotoxic and non infliction

Cost effective

Pharmacologically and physiologically inert

No interference with drug bioavailability

Should be effective at low concentration

The potency of oral absorption of aforementioned drug from such sort of formulation depends on several formulation-related parameters, like surface-active agent concentration, oil/surfactant magnitude relation, polarity of the emulsion, drop size and charge

The excipients are chosen relying upon the organ. Oil part is chosen looking on drug solubility in oil.

Surfactant is chosen supported the HBL worth.

The formulation of emulsion contains

Emulsifying agent
Antioxidant
Buffering agent
Preservative
Solvent
Co – solvent
Flavouring agent
Vehicle
Antimicrobial agent

Emulsifying agents

An emulsifying agent is Associate in Nursing associate material that enhances the soundness of an emulsion (i.e. bar of coalition and reducing creaming).

The ideal emulsifying agent is colourless, odourless, tasteless, non- toxic, non-irritant and able to manufacture stable emulsions at low concentrations.

An ideal emulsifying agent ought to possess the subsequent characteristics:

It should be able to reduce the interfacial tension between the two immiscible liquids.

It should be physically and chemically stable, inert, and compatible with the other ingredients of the formulation.

It ought to be non-irritant and non-toxic within the conc., used.

It ought to be organoleptically inert i.e. mustn't impart any colour, odour or style to the preparation.

It ought to be able to manufacture and maintain the desired viscousness of the preparation

Antioxidant

An inhibitor could be a molecule that inhibits the oxidisation of different molecules.

Oxidation could be a chemical process that may turn out free radicals, resulting in chain reactions which will harm cells.

It is accustomed forestall degradation by oxidisation

Hydrophilic- Lipophilic Balance (HLB)

HLB: the magnitude relation between the deliquescent parts of the molecule to the lipotropic portion of the molecule. The upper the HLB price of AN agent the additional deliquescent it'll be. The relative importance of the deliquescent and lipotropic teams was initial recognized once victimization mixtures of surfactants containing variable proportions of an occasional and high HLB variety. The potency of any combination (as judged by section separation) was found to pass a most once the mix contained a specific proportion of the chemical agent with the upper HLB variety.

HLB

Non ionic surfactant
Ionic surfactant
Calculation of HLB

Griffin equation is given by,

HLB=20(1 – S / A)

S: it is the saponification number of the ester

A: it is the acid number of the fatty acid Davis equation:

HLB = Hydrophilic group number + Lipophilic group number + 7

Buffering agents

These are materials which, when dissolved in solvent will enable the solution to resist any change in pH after an acid or an alkali is added.

The alternative of appropriate buffer depends on the hydrogen ion concentration and buffer in capability needed.

It is used to prevent a rapid change in pH when acids or bases are added to the solution.

Preservatives

Preservatives are agents that are commonly added to various foods and pharmaceutical products.

Helps to prolong their shelf life.

It is use to protect products from microbial contamination.

Solvents and co-solvents

A solvent is a substance that dissolves a solute, producing a solution. Co-solvent is a solvent that in conjunction with another solvent can dissolve a solute. It is used as they provide molecules to build some drugs.

In case of other drugs, solvents are used mainly for extraction and purification.

Flavouring agent

Our pharmaceutical flavours are available in liquid or powder form, in a variety of concentrations,

formulations and sizes. Flavours may be natural or artificial.

Used to mask unpleasant flavour and to improve the acceptance[5,6].

FORMULATION OF EMULSION

A pharmaceutical formulation is that the method within which totally different chemical substances as well as the active pharmaceutical ingredient square measure combined to supply a final product.

METHOD OF FORMULATION

A mortar and pestle is employed frequently in the extemporaneous preparation of emulsion. It is not a very efficient technique and cannot be used on a large scale. An emulsion is usually prepared by shaking strongly the mixture of the two liquids or by passing the mixture through a colloid mill known as the homogenizer. The emulsions prepared using pure liquids are unstable and the two liquids will separate during standing. Emulsions may be prepared by various methods, which depends upon the nature of the components and the equipment used. In case of pharmacy or laboratory i.e. Small scale, emulsions may be prepared using a dry Wedgwood or porcelain mortar and pestle or a mechanical blender or mixer that are comparatively simpler to use. On a large scale, large mixing tanks may be used to form the emulsion through the action of high-speed impellers. The types of equipment's can be divided into 4 categories

Mechanical stirrers

Propeller mixers - Homogenizers, Turbine mixers

Colloid mills

Ultrasonifiers

Mechanical stirrers

An emulsion can be stirred by means of various impellers. These impellers are mounted on shafts, which are placed directly into the system to be emulsified, i.e., the emulsion. Simple top entering propeller mixers are adequate for routine development work in the laboratory and production. This is used for mixing, suspending, milling, dispersing and reduces batch time.

Propeller mixers

The degree of agitation is controlled by propeller rotation but the pattern of liquid flow and resultant efficiency of mixing are controlled by the type of impeller, its position in the container, the presence of baffles, and the general shape of the container. These stirrers cannot be used when vigorous agitation is needed, extremely small droplets are needed and Foaming at high shear rates must be avoided.

Silverson homogenizer

An emulsion is also stirred by suggests that of varied impellers mounted on shafts, that square measure placed directly into the system to be blended. In homogenizers the dispersion of 2 liquids is achieved by forcing their mixture through a tiny low body of water passageway at massive pressures. The key to making a stable emulsion is getting the best attainable droplet size. The additional shear energy introduced into the combo, the smaller the suspended droplets can become, making a fine stable emulsion. Finer emulsions all the way down to 0-5 microns may be obtained, looking on the formulation. In several cases, this may eliminate the requirement for top pressure homogenizers. Silverson offers a variety of in-tank and In-Line mixers that are widely used for preparation of emulsions, from laboratory rescale to bulk production units.

Turbine type mixers

If more agitation is required or viscosity is more this can be used.

Colloid mills

They operate on a principle of high shear which is normally generated between rotor and stator of the mill. Colloid mill consists of a fixed stator plate and also a high speed rotating rotator plea which can rotate at a high speed. Materials such as the dispersions are usually drawn or pumped through an adjustable gap set between the rotor and stator is homogenized by the physical action and the centrifugal force which is created by high rotation of the rotor.

Ultrasonifiers

Ultrasonic energy is used to produce pharmaceutical emulsions. These transduced piezoelectric have limited output and are expensive. The system work very well with fluid of moderate viscosity giving extremely fine particle. The dispersion is forced through an orifice at modest pressure and is allowed to impulge in blade. The pressure range is from 150-300psi. This pressure causes blade to vibrate rapidly to produce an ultrasonic note. When the system reaches steady state, a cavitational field is generated at the leading edge of the blade[8,4].

EVALUATION OF EMULSION

Emulsions are mainly evaluated for their chemical and physical stabilities.

Chemical stability study involves the study of degradation of active drugs, emulsifiers, preservatives, anti-oxidants etc. Chemical instability can also leads to physical instability.

Physical stability study indicates the retaining of the integrity of the dosage form during shelf life. An emulsion is considered to be physically stable, if it can restore its initial properties on moderate shaking.

Optical transparency

Optical transparency of the formulation was determined by visually inspecting using naked eyes by inspecting the sample in clear and transparent container under the presence of good light and it is viewed against a black and white illuminated background.

Determination of pH

pH is usually measured using a pH meter of a glass electrode. pH fundamentally represents the value of hydrogen ion activity in solutions.

Procedure

A defined amount of formulation was taken and diluted with calibrated distilled water and mixed well. The electrode of the pH meter was immersed in the prepared formulation whose pH is going to determine. About 2gm of formulation was dispersed into 20ml of distilled water and by using a pH meter the pH is measured.

Viscosity Measurements

Brookfield viscometer is mainly used to determine the viscosity of the dispersion. Viscosity is the measure of fluid friction which might be considered as the internal friction resulting when a layer of fluid is made to move in relationship to another layer. Viscosity is a magnitude of the ratio of shearing stress to rate of shear.

Poise = Shear Stress (dynes)/ Rate of Shear (cm/sec)

Mechanical stress study

The chemical and physical stability of emulsion with were evaluated via phase separation by mechanical stress study. The emulsion formulation was centrifuged using a Remi centrifuge at 2000rpm for different time interval such as 10min, 30min, and 60min and noted down the volume of phase separation of formulation.

Particle shape and surface Morphology: Transmission Electron Microscopy (TEM)

Morphology and structure of the emulsion were studied using transmission electron microscopy. Here a drop of emulsion was suitably diluted with a small amount of water and it is applied on a carbon-coated grid, and a drop of 2% phosphotungstic acid was added and left for 30sec. The coated grid was dried under a vacuum and then taken on a grid holder and observed under the transmission electron microscope for its particle shape and morphology.

Atomic Force Microscopy (AFM)

An atomic force microscope is an excellent for visualizing particles with sizes ranging from 1nm to 10μm. Another advantage of the AFM is that its operation is very simple and that the AFM requires minimal sample preparation. It is possible to make quantitative measurements of particle size with an AFM. It can easily determine particle sizing parameters as long as the particle is > 100nm. If the particle size is less than 100nm special considerations are usually taken into account.

Particle Size Measurement

Determination of particle size distribution by particle size analyser: The selected best formulations were subjected to laser particle counting method. Samples are injected in the

sample delivery and controlling chamber. Following that, suitable solvent was pumped into the chamber. Now a beam of light were allowed to fall on the sample. When needed variety of runs, they were directed towards the detector. From this the particle size range and the average mean particle size of the formulation can be detected. The average particle size of emulsion formulations can be determined using another method - particle size analyser.

Procedure

Drug content analysis: 1ml of emulsion formulation was transferred into a beaker containing 10ml of methanol. The content of the beaker were stirred for approx. 30 minutes and then kept it for 24hr. After 24hr the content of beaker was transferred into centrifuge tube and it is centrifuged at the 3000rpm for 10 min. Supernatant was separated and it is filtered. Then 0.1ml of the supernatant was diluted appropriately with phosphate buffer saline (PBS) pH 7.4 and it is assayed spectrophotometrically for drug content.

Rheologic properties of emulsions

Emulsions are evaluated for its flow behaviour. Emulsion performance can be improved by the following flow related characteristics:

Removal of an emulsion from a tube or a bottle.

Emulsion – flow through a hypodermic needle.

Spread ability of an emulsion on the skin.

During manufacture (milling, etc.), stress can cause flow changes.

Spreadability of emulsion

For the determination of Spreadability excess of sample was applied in between two glass slides and that was compressed to uniform thickness by placing 1000 gm weight for 5 minutes. The time which is required to separate the two slides i.e., the time in which the upper glass slide moves over the lower glass slide was taken as measure of Spreadability **(**s).

$S = m \times l/t$

Where; m=weight tide to upper slide, l=length moved on glass slide, t=time taken[9,8,4].

Stability studies of emulsion

Stability studies should be established particularly for those active pharmaceutical ingredients which are likely to deteriorate on storage. During these elevated temperatures are used to determine the products shelf-life. This helps the patient to be cured easily and the acceptance of the drug would be easy and the known therapeutic uses of the pharmaceutical products manufactured. The emulsion should be physically and chemically stable and there should not be any bacterial growth during it shelf life. In the accelerated stability studies mainly, the drug is performed at long-term storage condition, an emulsion is said to be stable if it remains as such after its preparation that is after a moderate amount a shaking it should redisperse to its original form, i.e., During storage of dispersion medium, disperse globules are uniformly distributed.

Real-time stability testing

Accelerated stability testing

Retained sample stability testing

Cyclic stress stability testing

Real-Time stability testing

A real-time stability test is generally conducted for a longer period in order to allow for significant product degradation under already recommended storage conditions, The data collection is done at a time-to-time interval so that a trend analysis of the data can distinguish between stable and unstable conditions. Test duration is determined primarily by the stability of the substance, which must remain constant from one run to the next in order to indicate clearly that no measurable degradation occurs and to distinguish between inter-trial variation and degradation.

Accelerated stability testing

This normally provides an early hint of the product shelf life and so curtailing the development schedule. When testing accelerated stability, additional stress conditions are applied, such as humidity, light, agitation, intent, pH and package. This information is either projected to forecast shelf life or used to compare the relative stability of dispensable phrasings. During accelerated stability testing, a product is stressed at several high temperatures (warmer than ambient) and the amount of heat input alleged to cause failure is determined.

This is done to subject the product to a condition that accelerates degeneracy.

Design of the stability testing programme should take into account the intended call and the climatic conditions in the area in which the medication product will be used. Stability testing four climatic zones can be distinguished for the purpose of the world wide stability testing as follows,

Zone 1 is Temperature

Zone 2 is Subtropical, with possible high humidity.

Zone 3 is hot or dry

Zone 4 is hot or humid

It is recommended that stability testing programmes should be based on conditions corresponding to climatic zone 4.Since Since there are only a few countries in zone 1 the manufacturing would be well advised to base stability testing on the conditions in climatic zone 2 where it is intended to market products in temperate climates for countries where certain regions are situated in zones 3 or zone 4 and also with a view to the global market.

Retained sample stability testing

In this study, the stability samples are tested at predetermined or different intervals of time i.e., if a product has shelf life of 5 years, it is conventional to test the samples at different intervals of time i.e. here 3, 6, 9, 12, 18, 24, 36, 48, and 60 months are usually taken.

Cyclic temperature stress testing

For marketed products this is not a routine testing method. By design, cyclic temperature stress tests mimic likely market conditions in terms of demand and storage as closely as possible. In the most common scale, a cycle of 24 hours is considered, because the diurnal rhythm on Earth is 24 hours, which is the most common experience that marketed pharmaceuticals have during storage[2].

STORAGE

Emulsions should always be stored in a container with an airtight seal, protected from light, high temperatures or freezing

The emulsions are needed to be in cool place.

Light sensitive products or emulsions are mainly packed in amber coloured bottles.

For viscous or thick emulsions, a wide mouth bottles should be used.

Keeping emulsions at a cool temperature is best, but refrigeration is not advisable since this can adversely affect the stability of the preparation[9,10].

PACKAGING AND LABELLING

Container closure system for active pharmaceutical ingredients should be such that: its materials of construction will not have any effect on the ingredient.

Will give adequate protection against external influences: Will give adequate protection against potential contamination. Written specifications should be available for packaging materials.

Sound packaging procedures should be adapted to ensure that correct labels are affixed to the containers.

Labelling should contain that these drugs should be shaken thoroughly before use.

Special labelling advice

Shake well before use

Store in a cool place

Expiry Date

For external use only

Store in a cool dry place

Packaging materials

Mainly glass and various grades of plastics are used in packaging of emulsion.

Glasses such as borosilicate glass and soda lime are used and amber colored are also used in case of light sensitive products.

The usage of Plastic as packaging material in case of sterile as well as non sterile emulsions is increased[7,10].

DOCUMENTATION

Documentation is an important aspect in pharmaceutical industry irrespective of the fact that the manufacturing plant is involved in the production of formulation of dosage form or active ingredient

Master formulae

Master formula for each active pharmaceutical ingredient being produced should be available. The

master formula should include, master formula number starting materials, packaging materials, quality and quantity of starting and packaging materials, written instructions covering each stage of production, storage and quality control, signatures of responsible person and dates, date of effectiveness.

The copy should be retained for reference.

Batch documentation

Batch documentation is the most important documentation. This documentation consists of batch manufacturing record of each batch of intermediate products and of active pharmaceutical ingredient.

Standard operating procedure (SOP)

It is a set of written instructions that document a routine or repetitive activity which is followed by the employees in the organization. The developments of SOPs are an integral part of successful quality system. In order to achieve the predetermined specifications and a quality outcome, this information helps to perform a job effectively and consistently.

Quality audit plan and reports

Conducting internal audit and external audits of suppliers and outscoring operations are key elements of a good quality system .one asset of quality system that us identified recently released international conference of harmonization, pharmaceutical quality system, and in other quality system standards such as ISO 9001 is that conducting audits as a mean of evaluating complaints with the objective of quality system. ICH Q10 contains the implementation of quality management system model result in the achievement of three main objectives stated in ICH Q10 achieve product realisation, establish and maintain a state of control and facilities continual improvement.

Distribution records

The handling, storage and distribution of such products are often handled by various individuals and entities.

Table No.1: Formulations and Suspension[7]

Emulsifying agents/ Emulsifiers	a. Natural emulsifying agents	from vegetable source	Gum acacia, Karaya gum, Tragacanth Gumagar, Pectin, Guar gum, Soyabean
		from animal source	Gelatin, Egg yolk, Casein, Wool fat, Serum albumin
	b. Semi-synthetic polysaccharides	___	Methyl cellulose Carboxy methyl cellulose, cellulose, Hydroxy propyl methyl ,cellulose, Micro crystalline cellulose, Sodiumcarboxymethyl
	c. synthetic substances	Anionic	Sodium lauryl sulphate, Polypeptide condensates, Trioleyl phosphate, Sarcosinates,
		Cationic	Alkoxyalkylamines, Benzalkonium chloride, Cetrimide, Benzethonium chloride.
		Non -ionic	Polyoxyethylene, polyoxyethylene alkyl ethers, Polyoxypropylene, Sorbitan ester, Glyceryl ester, Sucrose esters, Polyoxyethylene fatty acids ester.
	d. Inorganic substances	___	Magnesium oxide, Milk of magnesia, Magnesiumtrisilicate, Magnesium aluminium silicate, Bentonite

	e. Alcoholic beverages	——	Polyethylene glycols (Carbowaxes), Cholestrol, Lauryl alcohol, Lecithins
Preservatives	Emulsion prepared by using different emulsifying agents, carbohydrates, proteins, non-ionic surfactants	—	Benzoic acid (0.1-0.2%) Chloroform (0.25%) Methyl Paraben (0.1-0.2%) Propyl Paraben (0.1-0.2%) Cetrimide (0.002-0.01%) Sodium benzoate
Anti-Oxidants	Oil and fats undergo oxidation	—	Tocopherol, gallic acid, ascorbic acid, propylgallate, citric acid, catechol, ethylgallate, pyrogallon
Flavouring Agents	Prevent unpleasant taste of some fixed oils and Emulsifying agents	—	Vanillin, benzaldehyde and aromatic water such as chloroform water, peppermint water, cinnamon water.

Table No.2: Test conditions for stability conditions

S.No	Environment	Sampling time points (Months)	Method and Climatic Zone
1	25°C/60% RH	3, 6, 9, 12, 18, 24, 36	Long term for zones I and IV
2	30°C/35% RH	3, 6, 9, 12, 18, 24, 36	Long term for zones III
3	30°C/65% RH	3, 6, 9, 12, 18, 24, 36	Long term for zone IVa, or intermediate condition for zones I and II
4	30°C/75% RH	3, 6, 9, 12, 18, 24, 36	Long term for zone IVa, or intermediate condition for zones I and II
5	40°C/75% RH	3, 6, 9, 12, 18, 24, 36	Accelerated condition for all zones

Table No.3: Types of stability studies

S.No	Types of stability studies	Storage conditions	Minimum time period (Months)
1	Long term	25±2°C and 60±5% RH or 30±2°C and 65±5% RH	12
2	Intermediate	25±2°C and 60±5% RH	6
3	Accelerated	40±2°C and 75±5% RH	6

Figure No.1

Figure No.2: Mechanical stirrers

Figure No.3: Propeller mixers

Figure No.4: Silverson homogenizer

Figure No.5: Colloid mills

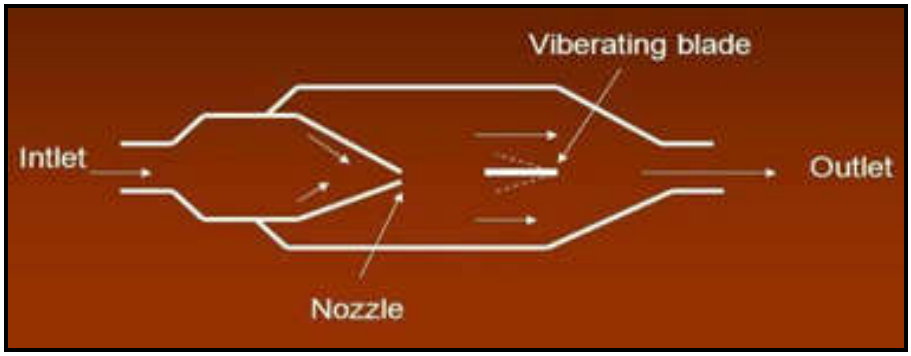

Figure No.6: Ultrasonifiers

Figure No.7: Storage

Figure No.8: Packaging and labelling

Figure No.9: Packaging materials

CONCLUSION

Emulsions are biphasic system, where immiscible liquids is finely subdivided and uniformly dispersed as droplets throughout another liquid with the help of emulsifiers.

Emulsions are very important in everyday life's huge number of products from food to cosmetics deal with emulsion such as milk, butter, creams, shampoos etc.

Stability studies can be related to many factors such as phase ratios, surfactants, temperature and other compounds in the systems.

The shelf life of a pharmaceutical product is critical. It must remain fresh, elegant and professional at all times. Since some products are portioned in multiple potion vessels, uniformity of potion of the active factor over time must be insured.

The active factor must be available to the case throughout the hoped shelf life of the cap. A breakdown in the physical system can lead to non-availability or of the medication to the patients[4].

ACKNOWLEDGEMENT

The authors wish to express their sincere gratitude to Malik Deenar College of Pharmacy, Seethangoli, Bela, Kerala 671321, India for providing necessary facilities to carry out this review work.

CONFLICT OF INTEREST

We declare that we have no conflict of interest.

REFERENCES

1. Mehta R M. Pharmaceutics II, *Vallabh Prakashan,* 4th Edition, 2017.
2. Sweeta Akbari, Abdurahman Hamid Nour. Emulsion types, stability mechanisms and rheology - A review, *International Journal of Innovative Research and Scientific Studies (IJIRSS),* 1(1), 2018, 14-21.
3. Sharma P P. How to practice GMPS, 5th Edition, 317-319.
4. Pooja Sonakpuriya, Mithun Bhowmick, Girijesh Kumar Pandey, Amit Joshi, Balkrishna Dubey. Formulation and evaluation of multiple emulsion of Valsartan, *International Journal of Pharm Tech Research,* 5(1), 2013, 132-146.
5. Excipients used in the formulation of liquid dosage forms, *Pharmaceutical Technology, Pharmaceutics,* 2020.
6. Md. Akhlaquer Rahman, Arshad Hussain, Md. Sarfaraj Hussain, Mohd. Aamir Mirza, Zeenat Iqbal. Role of excipients in the successful development of self emulsifying or microemulsifying drug delivery system, *Drug Development and Industrial Pharmacy,* 39(1), 2012, 1-19.
7. Sanmathi B S, Kalpesh K Mehta, Anshu Gupta. Dispensing pharmacy, a practical manual, *BSP Books,* 3rd Edition, 2018, 319-320.
8. Khar Roop K. Lachman and Leberman's the theory and practice of industrial pharmacy, *CBS Publishers and Distributors,* 4th Edition, 2021, 416.
9. Subrahmanyam C V S. Textbook of physical pharmaceutics, *Vallabhprakashan,* 2nd Edition, 2000, 395-426.
10. David Jones. Pharmaceutics dosage form and design, *Pharmaceutical Press,* 2008, 296.
11. Allen. Ansels pharmaceutical dosage form and drug delivery system, *Wolters Kluwer India Pvt. Ltd,* 11th Edition, 2018, 404-409.
12. Patrick J. Sinko. Martins physical pharmacy and Pharmaceutical science, *Lippincott Williams and Wilkins,* 7th International Edition, 2016, 672.

Please cite this article in press as: Mahitha *et al*. Formulation and characterisation of emulsion, *International Journal of Research in Pharmaceutical and Nano Sciences,* 10(5), 2021, 316-329.