

An Overview on Nanoemulsion: Different aspects, formulation and evaluation parameters

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Received 05-05-2023	Abstract. Nanoemulsions are well known formulation for immiscible Pharmaceutical products. In the modern era Nanoemulsion formulation are growing very fast. This is important to understand the benefits preparation techniques, methodology, equipments, machinery and many more to improve Nanoemulsion. In the Nanoemulsion various types of low energy emulsification techniques like high pressure homogenization, ultrasonication and microfluidization techniques are used to formulate. Due to Nanoemulsive particles, the absorption rate of drug in nanoemulsion is higher in the body. It also enhance the bioavailability of the drug. Thus this can be said that the immiscible drug in nanoemulsion is more effective than other dosage form.	Keywords: Nanoemulsion, Surfactant, Co-surfactant, Bioavailability, Nano size droplet, Homomixer
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INTRODUCTION

Nanoemulsion is the ratio of surfactant, co-surfactant and aqueous phase which is emulsified in oil phase. All these particles are colloidal dispersed in the nanoemulsified mixture. Nanoemulsion aim to be achieve higher bio-availability so drug should be readily and completely absorbed to produce high efficacy of drug. In the formulation of nanoemulsion drug substances are converted in the nano size droplet (1- 100 nm).

Nanoemulsion are made up of two or more immiscible colloidal isotropic submicron, ultrafine particle system in the mixture with surfactant, co-surfactant to finalize in one phase.

Benefits of Nanoemulsion:-

- To reduce the absorption mutability.
- To achieve lipid fat substance solubility.
- To reduce the gritty taste.
- Help to achieve wide distribution by various routes (topical,oral,IV).
- To gain fast and quick access of drug in the body.
- Nanoemulsion have mightiness to mix huge amount of hydrophobic compounds.
- It has ability to produce standard Drug Delivery System.

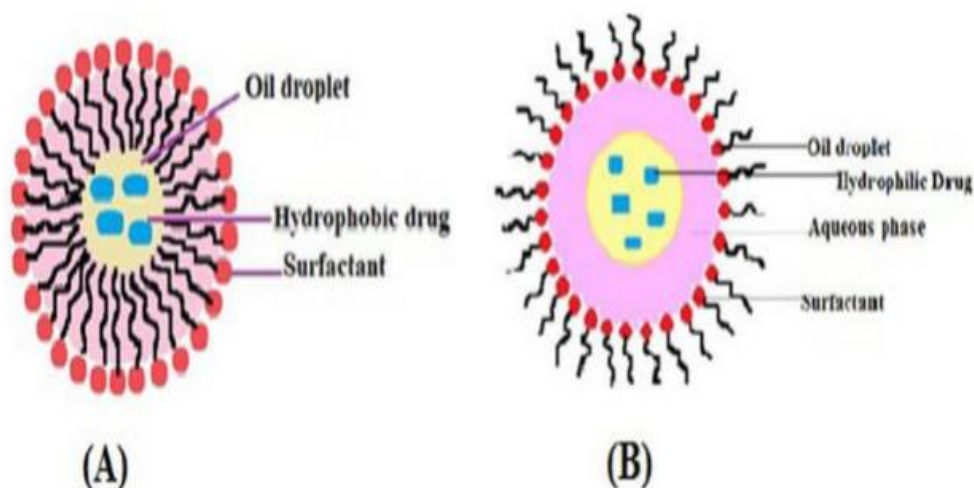
- It is irritation free and non toxic.
- It uplifts the bioavailability of drug.
- It is present in various formulation i.e. foams, creams, sprays and liquids.
- To hide the real taste.

Disadvantage of Nanoemulsion:-

- Without surfactant and co-surfactant emulsion doesn't stable.
- Temperature and pH like atmospheric factors affects the nanoemulsion's stability.
- Nano droplets present in emulsions is required high quantity of surfactant as well as co-surfactant for stability.
- The additional matters which have high melting point produce rate limiting solubility capacity.
- Environmental circumstances like temperature affects the nanoemulsion durability.

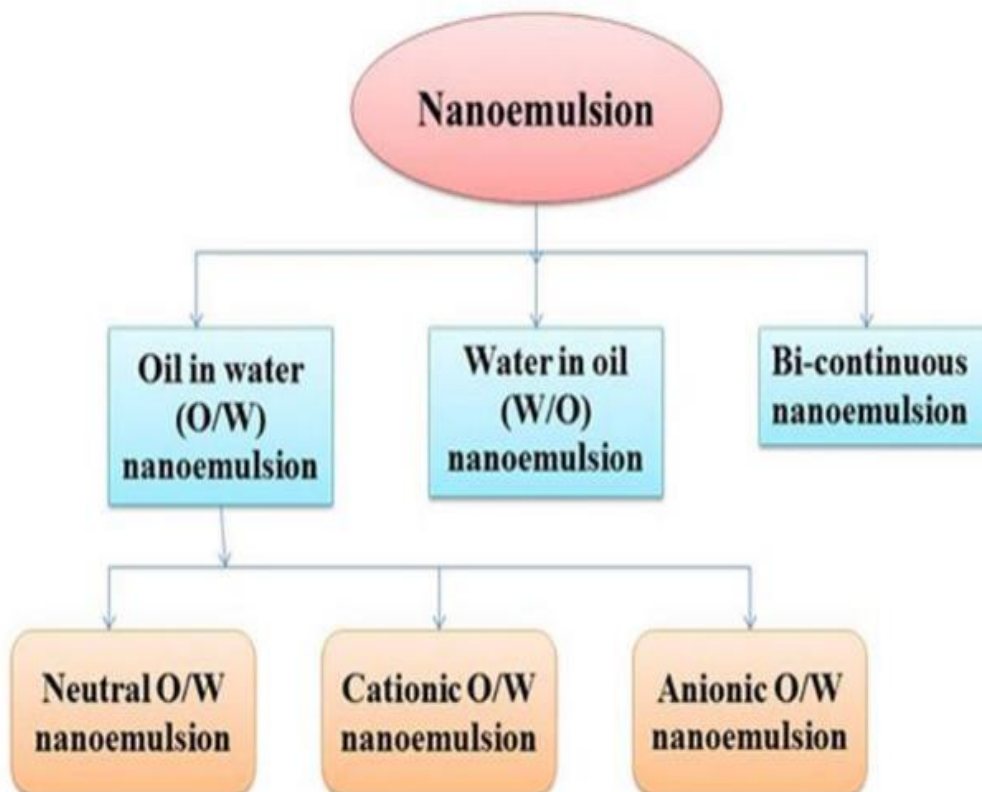
Taxonomy of nanoemulsion:-

- Oil in water (O/W)nanoemulsions (oil droplets dispersed in aqueous phase)
- Water in oil (W/O)nanoemulsions (water droplets dispersed in oil phase)
- Bi- continuous nanoemulsions (oil and water inter dispersed within the system)



In the study of Nanoemulsions with transdermal drug delivery system nanoemulsion shows pseudo tertiary phase. For identify the qualitative and quantitative parameters of nanoemulsion particles is done with the help of Transmission electron microscope. This also helps in evaluation of

stability studies, in-vitro permeation study, refractive index, droplet size distribution etc. All these studies shows that nanoemulsion on transdermal delivery system producing good drug delivery in various disease like rheu.Arth., inflammation and pain.



Differences in Nanoemulsion and Emulsion:-

- Nanoemulsion measured 1- 100 nm while emulsion is 1 -20 micrometer.
- Nanoemulsion are clean and constant while emulsions are hazy unconstant and hasa sedimented particles.

- Nanoemulsion are kinetically stable while emulsions are kinetically very low stable.

Preparation techniques of Nanoemulsion:-

There are two techniques which are used to formulate Nanoemulsion:-

High energy emulsification technique:-

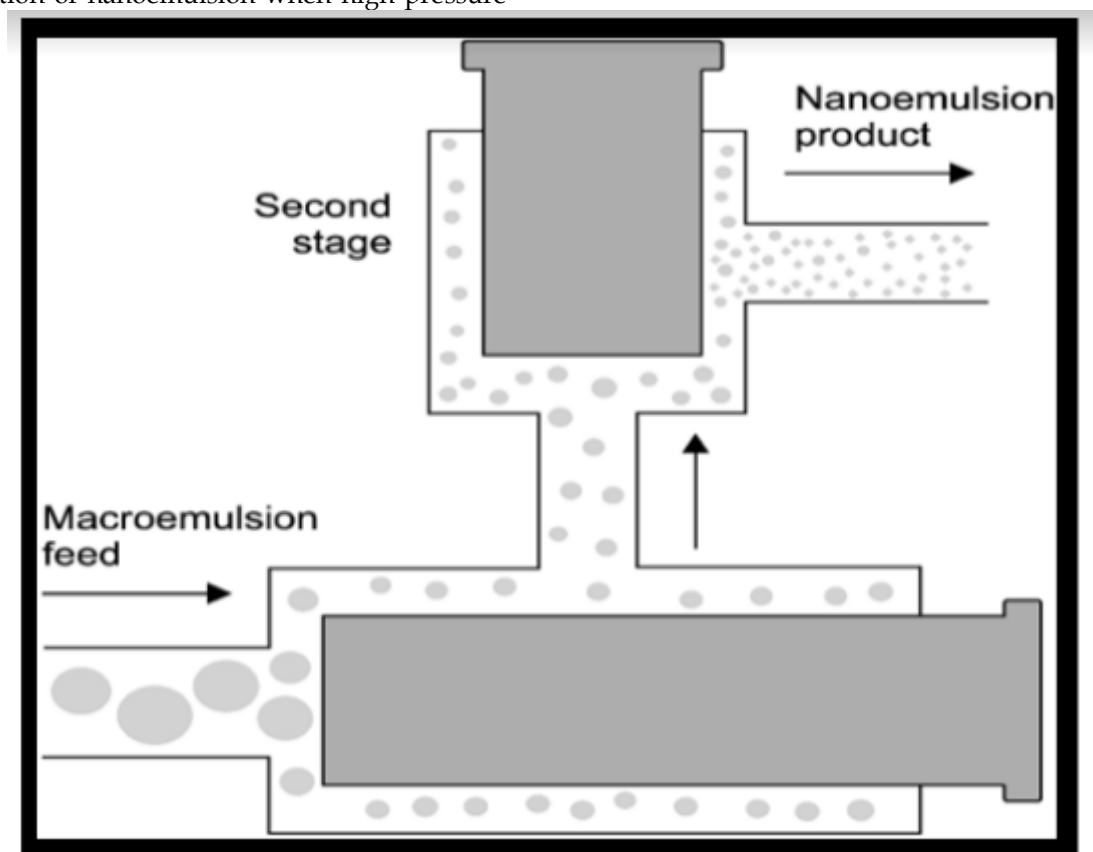
- (A) Membrane emulsification
- (B) High pressure homogenization
- (C) Ultrasonication
- (D) Microfluidization

Low energy emulsification technique:-

- (A) Solvent evaporation technique
- (B) Emulsion phase inversion point technique
- (C) Hydrogel technique
- (D) Spontaneous emulsification techniques
- (E) Phase inversion temperature

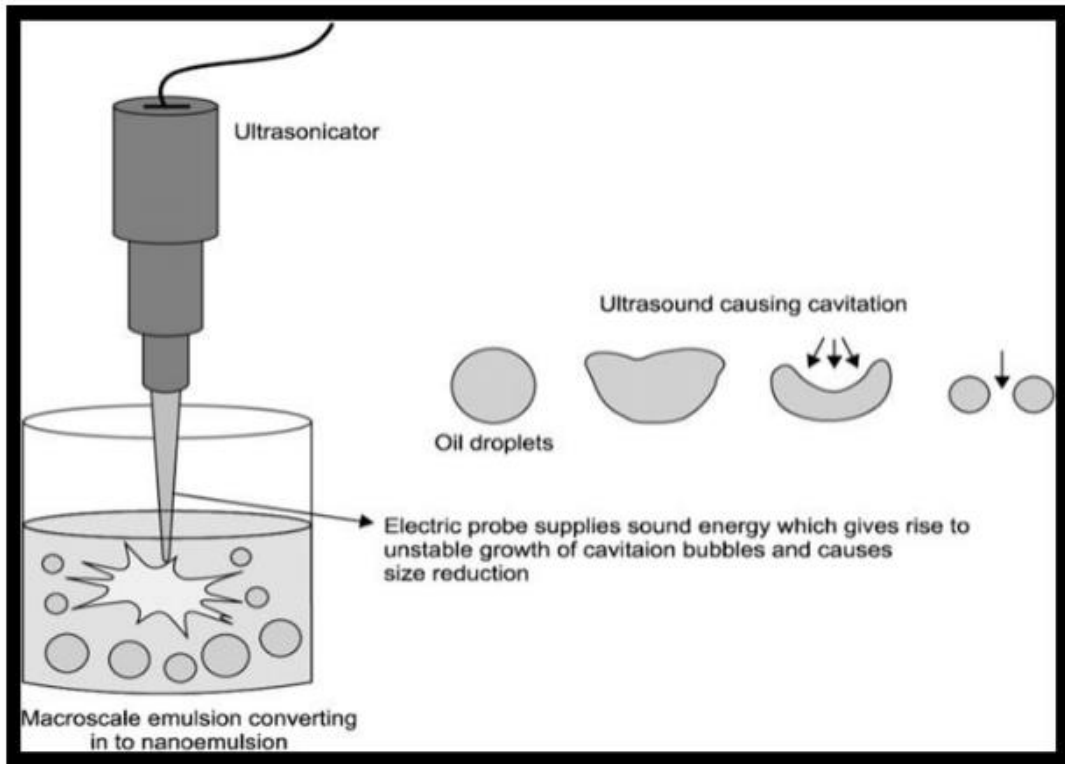
High pressure homogenization:- Approximately 1 nanometer droplet size may be prepared in the formulation of nanoemulsion when high pressure

is applied on oil phase and water phase. Even if the required droplet size may be prepared this method is applied to reduce the droplet size when the quantity of homogenization cycle is enhanced. To produce submicron particles high energy is required various steps procedure formulations are used to elevate the strength of emulsification. With the help of high over the system with aqueous phase, oil phase, co surfactant and surfactant this method is used. Homogenizer is widely used to perform pressure on nano particles during the homogenization step few barrier are affecting like component degradation, fortuneless productivity etc. which direct affected the generation of more heat.



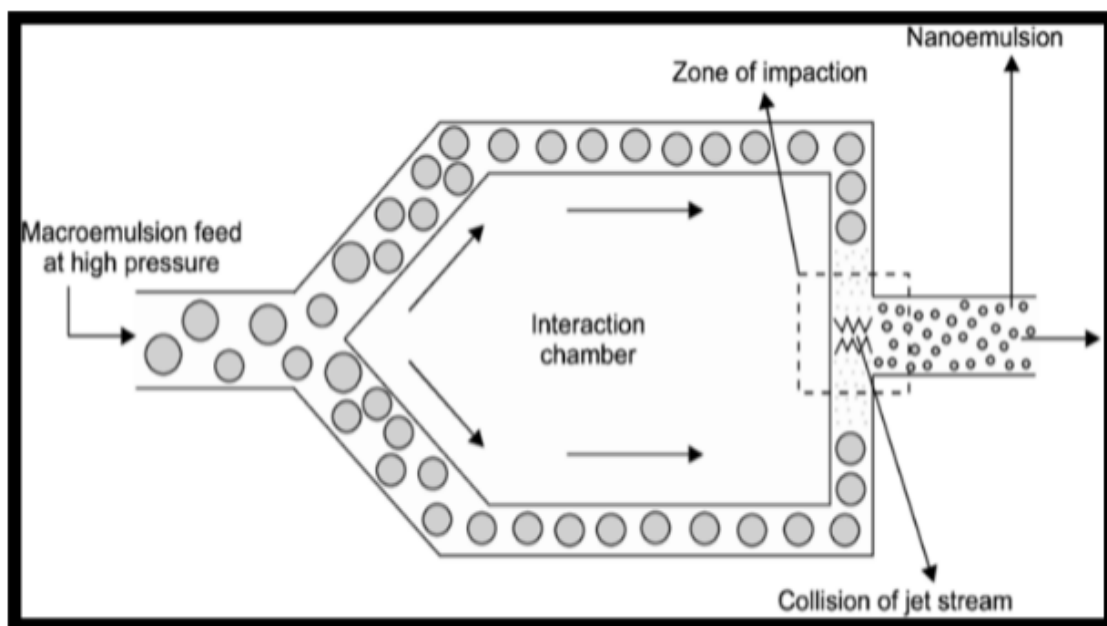
Ultrasonication method:- To agitate the nanoemulsion particles in minimal quantity most preferably method is ultrasonication. Ultrasonication technique help in nanoemulsive droplet size reduction. Sonicator is small scale equipment so only few amount can be applied to formulate the nanoemulsive particles. Probe Sonicator also help in ultrasonication and sonication time plays an important role in the

nanoemulsive particles. Sonication method also applied in conventional emulsions reduce the droplet size of nanoparticles. Ultrasonicator converts the macromolecule into the nanoemulsion by the Ultrasonic waves. Acoustic Cavitation physical shear the particles in which cavitation creates the microbubbles to create pressure fluctuation.



Microfluidization:-In microfluidization technique large particles are move into smaller particles by microfluidizer in which more pressure creates enhance displacement pump through the product convert in bubbles to micro size. To start this process water phase and oil phase in coarse form are passed through microfluidizer so that they obtain nanoemulsion in great volume.

Microfluidizer have micro channels in interaction chamber through which have high pressure generated by displacement pump at 500 to 200 PSI. Submicron ranging particles are impingement by micro channels. When oily and aqueous phase are mixed with each other they producing coarse emulsive particles which further fluidize by microfluidizer.



Low energy emulsification technique:-
Phase inversion temperature method :- Research

shows that small particles (Nanoemulsion)

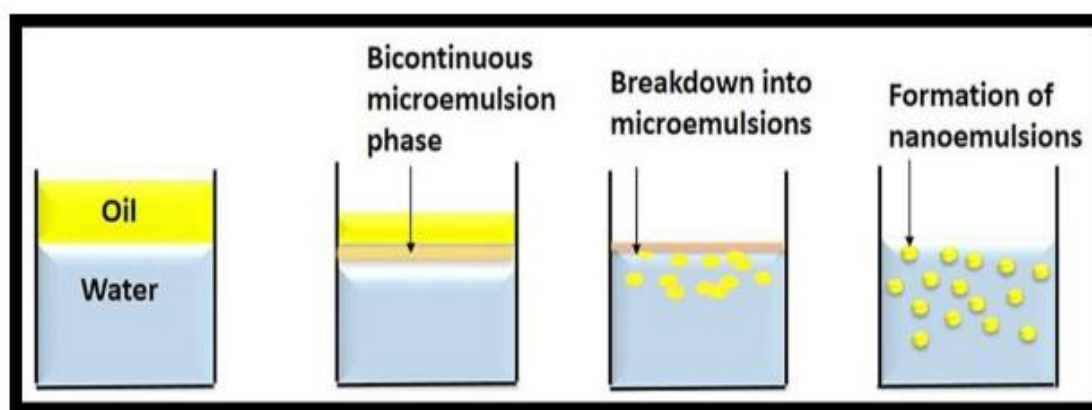
increases the durability so that particles doesn't sedimented, doesn't collected on upper surface and does not ostwald ripening which helps in good nanoemulsion preparation. There are two types i.e. transitional inversion and catastrophic inversion includes for the formulation of nanoemulsions. In this step the combination of non ionic water and oil are mixed. It decreases the deterioration of drugs which are thermodynamically unstable such as peptides and get tretinoin. In fact in phase inversion temperature method oil in water nanoemulsion changes into water in oil emulsion.

Phase inversion composition technique:- In this technique water mixed with oil at a very slow rate. In this technique organic solvent heat or sometime also prepared at room temperature. In phase composition technique droplet size is ranging from 40 - 60 nm. The PIC technique is relevant to PIT technique that's why this technique cognizable with modify the system composition in place system temperature. On slowly addition of water in oil phase and due to amount of water fraction gradually increases surfactant like Polyoxyethylene chain hydration occurs. The hydrogen and lipid loving character of water phase is getting equivalent spontaneous curvature of surfactant which getting change to zero similar to hydrophilic- Lipophilic balance temperature

within the phase inversion temperature method. In this step transition cause lamellar structure or bicontinuous structure is made. In case if more water is added then the transition temperature is increased and so that the structure of surfactant layer with zero curvature convert into elevated positive curvature.

Spontaneous emulsification techniques:- By mannerly stirring at required temperature when oil and water are mixed with the help of emulsifier is used then spontaneous emulsions are made in this method. To enhance oil droplet formation in aqueous phase most preferably magnetic stirrer is gently used to make homomixer. It involves three main steps:-

- Formulation of homogeneous organic solution which are composed of lipophilic surfactant as well as oil in hydrophilic surfactant in aqueous soluble solvent.
- Oil in water emulsion is made when the organic phase passes into water phase on magnetic stirring.
- When this step is applied under reduced pressure the aqueous solvent is eliminated with the help of evaporation.



Factors influencing in the formulation of Nanoemulsion :-

- It avoid in homogeneous mixture dispersed phase must be over much insoluble in dispersed medium.
- The surfactant must not be made liquid lyotropic crystalline 'Microemulsion' phase is the backbone of Nanoemulsion. The system which include short chain alcohols, water, alkanes and surfactant make the phases that are commonly used with the combination of cosurfactant.

- More surfactant emphasizes the fresh surface area which to be fastly wrapping during emulsification to completely stop the coalescence.
- On shearing of these micro size liquid droplets are converted from micro to nano size due to increase in laplace pressure stress level

Parameters used for the evaluation of Nanoemulsion :-

- **Droplet size analysis :-** A diffusion method by using a light dispersing particle size analyser

counter is used for the measurement of droplet size analyser of Nanoemulsion. Spectroscopy analyzing method used to determine/ analyse the nanoparticles by light scattering Brownian motion. With the help of TEM (transmission electro microscopy) may also be adhere to analyse droplet size of Nanoemulsion.

- **Viscosity determination** :-Brookfield Rotary viscometer is also help in viscosity determination at various temperature and various shear rate.
- **Dilution test:-** In this test nanoemulsion is diluted either with oil phase or water phase that helps in demonstration. In this test when much continuous phase will be added in nanoemulsion, it doesn't cause any circumstance in its stability.
- **Drug content:-** In this step with the help of spectrophotometer or high performance liquid chromatography opposite standard solution of drug the extract is analysed so that by using a suitable solvent is dissolved to extract pre-weighed Nanoemulsion.
- **Refractive index:-** Abbes type refractometer is an instrument which is used for the measurement of refractive index of nanoemulsion. The Abbes type of refractometer is used as 25 ± 0.5 degree Celsius to determine the refractive index.
- **pH** :-With the help of pH meter the nanoemulsion's pH may be measured and the actual pH of formulation is determined.
- **Zeta potential** :-Zeta potential analyser is an instrument which are used for the measurement of the formulation .This instrument measure the charge in nanoemulsions which are present on the surface of droplet.

CONCLUSION:-

Above mentioned such different aspects, formulation and evaluation parameters are the backbone for nanoemulsions development. Nanoemulsion development related techniques are linear growing with the time. Nanoemulsion provide more stability, larger surface area for absorption, prevention in coalescence due to nanoparticle size, immiscible particles are easily shear. it also provide many more advantages.

REFERENCES:-

- [1]. Halnor VV*1, Pande VV2, Borawake DD3, and Nagare HS3 Nanoemulsion: A Novel

- Platform for Drug Delivery System: Journal of Materials Science & Nanotechnology February 2018 Volume 6 (1) : 1-3
- [2]. Abdulelah FM, Taghi HS, Abdulbaqi HR, Abdulbaqi MR. Review on Nanoemulsion: Preparation and Evaluation. *International Journal of Drug Delivery Technology*. 2020; 10(1):187-189.
- [3]. Vibhu Khanna, Saurabh Singh*, Dileep Singh Baghel, Barinder Kaur, Alka Nayar, Rajiv Ghimire: NANOEMULSIONS - PRESENT AND FUTURE PERSPECTIVE - AN OVERVIEW: *Journal of Emerging Technologies and Innovative Research (JETIR)*: 2018: Volume 5(12):354-358
- [4]. Jyotsana Suyal * 1, Ganesh Bhatt 2 and Nardev Singh 1: FORMULATION AND EVALUATION OF NANOEMULSION FOR ENHANCED BIOAVAILABILITY OF ITRACONAZOLE: *International Journal of Pharmaceutical Sciences and Research*: Vol. 9(7): 2927-2931.
- [5]. Tushar Hemant Nikam, Mahesh Pralhad Patil, Snehal Sunil Patil, Gautam P. Vadnere, Santram Lodhi* : Nanoemulsion: A brief review on development and application in Parenteral Drug Delivery: *Advance Pharmaceutical Journal* 2018; 3(2): 43-54
- [6]. NASIM HESHMATI,1 XINLAI CHENG,2 GERHARD EISENBRAND,3 GERT FRICKER1 Enhancement of Oral Bioavailability of E804 by Self-Nanoemulsifying Drug Delivery System (SNEDDS) in Rats: *Pharmaceutics, Drug Delivery and Pharmaceutical Technology*: DOI 10.1002/jps.23696:1-7
- [7]. Sheikh Shafiq *, Faiyaz Shakeel, Sushma Talegaonkar, Farhan J. Ahmad, Roop K. Khar, Mushir Ali: Development and bioavailability assessment of ramipril nanoemulsion formulation: *European Journal of Pharmaceutics and Biopharmaceutics* 66 (2007)227-243
- [8]. R. Neslihan Gursoy a, Simon Benita b,* ,1: Self-emulsifying drug delivery systems (SEDDS) for improved oral delivery of lipophilic drugs: *Biomedicine & Pharmacotherapy* 58 (2004) 173-182
- [9]. Sunny Antil1, Chitra Gupta1: Formulation and Evaluation of Nanoemulsion for Bioavailability Enhancement of Metaxalone: *International Journal of Current Research and Review*: July 2021 :

- Vol 13 (14):47-52
- [10]. Abdhesh and Sanjiv Kumar Gupta: Formulation and Evaluation of Nanoemulsion Based Nanoemulgel of Aceclofenac: *Journal of Pharmaceutical Sciences and Research*: Vol. 12(4), 2020, 524-532
- [11]. Gunjan P. Malode*, Sarin A. Chavhan, Shivam A. Bartare, Lochana L. Malode, Jagdish V. Manwar, Ravindra L. Bakal: A Critical Review on Nanoemulsion: Advantages, Techniques and Characterization: *Journal of Applied Pharmaceutical Sciences and Research*. 2021; 4(3):6-12.
- [12]. Dony Lonappan*, K Krishnakumar, B. Dineshkumar: Nanoemulsion In Pharmaceuticals: *American Journal of Pharmtech Research* 2018; 8(2) : 2-8
- [13]. K. GURPREET AND S. K. SINGH* Review of Nanoemulsion Formulation and Characterization Techniques: *Indian Journal of Pharmaceutical Sciences*: September-October 2018: 781-787
- [14]. Ashwini Khare*, Afaque Ansari, Payal Patki, Nuseba Perampalli: DESIGN AND DEVELOPMENT OF NANOEMULSION FORMULATION: A REVIEW: *International Journal of Creative Research Thoughts*: Volume 9,(7) July 2021: b85-b93
- [15]. Raj Kumar Mishra, G. C. Soni, Rekha Mishra: Nanoemulsion: A Novel Drug Delivery Tool: *International Journal of Pharma Research & Review*, July 2014; 3(7):32-43