Determination of Pickering Nanoemulsion by Eudragit RL-100 Nanoparticle as Oral Drug Delivery for Poorly Soluble

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Authors’ contributions
This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

ABSTRACT

Objective: The purpose of this research study was to develop Ketoprofen-loaded Pickering nanoemulsion with the help of polymeric nanoparticles [NPs]. The pickering nanoemulsion formulation is developed using Eudragit RL 100, which has the greater ability to stabilize the formulation as well as it better controls the release of drug upon oral administration.

Method: In the present study, Ketoprofen-loaded Pickering nanoemulsion were prepared using an ultrasonic emulsification process. For the preparation of the Nanoemulsion, an aqueous phase of the nanodispersion of nanoparticle is used while Captex-300 and drug premix is used as oil phase. The nanoemulsion is formulated by using a probe sonicator with different ratios of aqueous phase and oil phase. The preformulation study of polymer or drug is done by FTIR and DSC and the drug-polymer compatibility was confirmed by FTIR. The prepared formulation was evaluated for physical appearance, pH, Viscosity, In vitro drug release, Particle size, Zeta Potential, Polydispersivity index, and transmission electron microscopy and stability. The Formulation is optimized for the different concentrations of the aqueous phase and oil phase with concentrations of drug and polymer.

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Results: All the prepared formulations show particle size in between 100-500nm hence it indicates formation of nanoemulsion. The zeta potential is -46mv which indicates good stability of formulation. The In vitro drug release shows maximum drug release i.e. 96.93% in 10 hrs which shows that the release of drug is prolonged due to formation of Polymer NPs.

Conclusion: Thus the drug release was significantly controlled and slowed down when nanoemulsion is formulated by using NPs in comparison with control. These results fulfilled the objective of the study. This study opens new prospects on the formulation of Pickering nanoemulsion.

Keywords: Pickering nanoemulsion; Ketoprofen; Eudragit RL-100; Captex-300.

1. INTRODUCTION

Pickering’s solid particle-stabilized emulsions were discovered by Ramsden and Pickering within the 1900s and developed slowly until the 1980s [1,2]. Compared to surfactant-stabilized emulsions, Pickering emulsions have shown the benefits of strong stabilization and really good coalescence resistance happens to the formation of a dense shell of solid particles irreversibly adsorbed around water droplet emulsions [3-5]. Pickering emulsions have generated considerable interest in research in several areas particularly within the cosmetic and pharmaceutical fields or food applications, where surfactants often have undesirable effects (such as irritation and hemolytic behavior) [6]. As a new drug delivery system, Pickering emulsions could facilitate dermal drug delivery increase the oral absorption of poorly water-soluble drugs and improve drug stability [7]. Recently, various Pickering nanoemulsions have been described. They have average droplet diameters within the range of 50–300 nm. The adsorption of solid particles at the water/oil interface is irreversible and strong.

Classical emulsion using surfactants has shown some undesirable characteristics in pharmaceutical applications. In most applications, Pickering particles can be substituted for surfactants in the classical emulsion [8-11]. Pickering emulsion using solid particle as an emulsifier may provide a way to avoid some undesirable side effects that can come along with using surfactant [12,13].

Ketoprofen is a non-steroidal anti-inflammatory drug. It belongs to BCS class II drug, that is high permeability low solubility [14]. It is used for the relief of pain and inflammation in rheumatoid arthritis, osteoarthritis and ankylosing spondylitis. It is administered orally and externally applied as a gel. The oral bioavailability is up to 60% [15]. The pickering nanoemulsion formulation is developed using Eudragit RL 100, which has the greater ability to stabilize the formulation as well as which better controls the release of drug upon oral administration.

2. MATERIALS AND METHODS

2.1 Materials

Ketoprofen was gifted from BEC Chemicals Pvt. Ltd, Roha, Raigad, Captex -300(MCT) was purchased from Abitech corp. Mumbai India, Tween 80 and Eudragit RL-100 polymer are purchased from Modern Science Nashik and all other chemical used were of analytical grade.

2.2 Preformulation Studies of Ketoprofen and Polymer [16,17]

Preformulation parameters are check for Ketoprofen and eudragit and it was characterized by organoleptic properties solubility melting point and compatibility studies by using FTIR Techniques.

2.2.1 FTIR Analysis

The dry sample of the drug was mixed with KBr within the ratio of 1:99. The sample was triturated and eventually placed in a sample holder and compressed employing a motorized pellet press at 15 tones pressure. The pellets were then scanned using an FTIR spectrophotometer (Shimadzu; IR Affinity-1S) over frequency ranges from 4000 to 400 cm⁻¹. The spectra were analyzed by comparing the standard ranges of functional groups [18].

2.2.2 Drug- Excipient compatibility Studies

A compatibility study was carried out in order to establish, that there was no interaction between the drug and excipients used in the formulation. The drug and physical mixtures of the drug: polymer (1:1) were filled in the vial and sealed.
The sealed vials were kept at a specific temperature (in a desiccator) for 45 days. After 1 month mixture evaluated by FTIR. The preliminary compatibility was carried out by FTIR (Shimadzu: IR Affinity-1S). The FTIR spectrum was recorded from 4500cm⁻¹. Infrared spectra of pure drug and physical mixture of drug with polymers were obtained by using standard KBr sample [18].

2.3 Method of Preparation of Pickering Nanoemulsion

2.3.1 Step –I
Preparation of nanoparticles by Nano precipitation method in which the organic phase and aqueous phase were mixed at different ratios. The organic phase is Eudragit RL100 and acetone and the aqueous phase is 1% of tween 80 in water. Then the Nano dispersion was prepared by adding of organic phase at a constant rate of 0.5 ml/min in an aqueous phase under gentle agitation. After that acetone was removed from it by a Rotary evaporator. Then Nano dispersion is concentrated by evaporating a significant amount of water. After that kept it for washing in spectra pore regenerated cellulose tubing with water by the gentle stirring for 48 hrs. Formula for preparation given in Table 1.

2.3.2 Step - II
Preparation of Pickering Nano emulsion by using this washed Nano dispersion with an oil phase containing Ketoprofen + Captex 300 (MCT) at different ratios. The premix of Drug + Captex is formulated using a mechanical mixer. Operating at 5000 rpm for 10 min, at 25°C. Then Nano emulsion is generating by using probe sonication. Formula for preparation given in Table 2.

3. CHARACTERIZATION OF NANODISPERSION AND PICKERING NANOEMULSION

3.1 Physical Appearance
The physical appearance of Pickering nanoemulsion was observed visually.

3.2 PH Determination
The pH of the Pickering NE formulation was determined by using a pH meter. For pH determination, 1% Pickering nanoemulsion formulation in deionized water was prepared and pH was determined [19].

3.3 Viscosity Determination
The viscosity is measured to determine the rheological properties of formulation by Brookfield viscometer at different rpm. The torque is set for 95% for all formulations so that we get constant readings of all formulations [20].

3.4 % Drug Entrapment Efficiency
To determine the percent drug entrapment drug efficiency, take 2ml of Pickering nanoemulsion of Ketoprofen and centrifuged at 12,000 rpm for 30 min. after centrifuge supernatant is obtained and diluted it with water (1:1) and after that analyzed by the UV-Spectrophotometry 257-260 nm [21,18,22].

The % entrapment efficiency is calculated by following equation.

\[
\% \text{ entrapment efficiency} = \frac{\text{Total drug} - \text{free drug in supernant}}{\text{Total Drug}} \times 100
\]  

(1)

3.5 In –vitro Drug Release of Pickering Nanoemulsion
The dissolution study is carried out using USP dissolution apparatus type-II (Paddle apparatus). The drug release study of Premix, Nanoemulsion formulation and Marketed film coated tablet formulation is measured by the dialysis tubing method. The premix of drug and Captex -300 and prepared Pickering nanoemulsion 2ml (8mg/ml) is filled in two tubes of dialysis membrane -50 (at Av. flat width -24.26 mm and Av. Diameter 14.3 mm). In order to simulate pH changes along with GIT, the dissolution medium with 0.1 N HCl and pH 6.8 buffer were sequentially used. When performing the in-vitro release experiments, 0.1 N HCL medium was first used for 2hr which was then replaced by fresh 6.8 pH phosphate buffer for a further 10 hrs. Samples were withdrawn at regular time intervals. Samples were estimated using UV-Vis Spectrophotometer (Shimadzu 2450 – double beam UV-Vis Spectrophotometer) at respective wavelengths [23].

3.6 Particle Size Distribution and Zeta Potential Measurement
Particle size distribution, zeta potential, and Polydispersivity index of nanodispersion and Pickering nanoemulsion were determined by
using a Malvern particle size analyzer. To check the stability of this nanoemulsion. The sample was diluted 3 times with distilled water before the experiment is performed at 25°C [19,24].

3.7 Transmission Electron Microscopy

Transmission electron microscopy was used to analyze the morphology of the nanoemulsion droplets. Samples were diluted 100 times with distilled water after dilution a drop of Samples were placed on the carbon- support than allowed to stand 5 minutes for drying and placed in the vacuum chamber for 30 minutes before analysis [23].

3.8 Stability Study

To evaluate the physical stability of the optimum formulated Pickering NE for ketoprofen, it was stored at 40 °C and 75% relative humidity (RH) in an oven for 90 days. The NE entrapment efficiency, Zeta Potential, Particle size were determined after one and three month’s storage.

4. RESULT AND DISCUSSION

4.1 Preformulation Study

The Preformulation study has been performed to determine the physicochemical properties of a drug. The melting point of Ketoprofen was found to be 94-97°C. The solubility of the drug is checked in three different solvents the results are given in Table 3 The solubility of ketoprofen determine in three different solvents was found to be soluble in ethanol and phosphate buffer 6.8 and poorly soluble in water [16,17].

4.1.1 FTIR analysis

FTIR analysis was done to check the possible interaction between drug and polymer. The Pure Ketoprofen spectra show characteristic peak at 1650cm⁻¹ is corresponding to amide N-H stretching, 1290cm⁻¹corresponding to amine C-N stretching,2900.01cm⁻¹ corresponding to carboxylic acid O-H stretching. The pure eudragit RL-100 spectra shows 1730cm⁻¹corresponding to aldehyde C=O stretching and 3085.35cm⁻¹ are corresponding to unsaturated system eg alkenes. The FTIR spectra shows the compatibility of Ketoprofen with Eudragit RL-100. The comparative spectra given are in Fig. 1.

4.2 Characterization of Nanodispersion and Pickering Nanoemulsion

4.2.1 Physical appearance

The appearance of the formulated Pickering nanoemulsion is transparent white. The image is shown in Fig. 2.

4.2.2 PH determination

PH of all formulation batches NE1-NE9 was determined by pH meter results are given in the Table 4.

4.2.3 Viscosity (in CP)

In the determination of viscosity of this, all formulation batches NE1 shown viscosity in between 380-1141, NE2 shown 370-1104, NE3 shown 369-1143, NE4 shown 360-1190, NE5 shown 390-960, NE6 shown 380-970, NE7 shown 360-1142, NE8 shown 365-950, NE9 shown 370-1050 from above the formulation batch NE3 shows good viscosity. Results are shown in Table 5.

4.2.4% Drug entrapment efficiency

The drug entrapment efficiency of all NE1-NE2 of the Pickering nanoemulsion formulation was determined for drug content in the formulation. The entrapment efficiency of all formulations is found to be in the range of 72.00 -92.20 %. From them, the Optimized formulation NE3 shows higher entrapment efficiency. Results are shown in Fig. 3.

4.2.5 In-vitro drug release study

a) Drug release from Marketed tablet and Premix (Ketoprofen +Captex -300)

This study is performed to study the effect of nanoparticles containing nanodispersion on the formulation to prolong the drug release of the drug. This marketed film coated tablet and premix is considering as control. The release of drug in tablet gives 92.78% in 3 hrs. and premix gives 100% in 2.5 hrs. Results are shown in Table 6 Fig. 4.
b) In vitro Drug release of ketoprofen loaded Pickering nanoemulsion

In this study, the dissolution of optimized batch NE3 was performed for 10 hrs. The release of ketoprofen loaded Pickering nanoemulsion at pH 1.2 is slower and by increasing the pH 6.8 of the release medium drug release is increase. The release of drug from Pickering nanoemulsion was found to be only 15 % of drug release within 2 hrs. And after 5 hrs. 70 % of drug release and finally 96% of drug release from formulation at 9 hrs. By comparing the Pickering nanoemulsion with control Marketed Tablet formulation and premix of (Drug + Captex -300) it clearly found that the effect of Eudragit RL-100 NPs significantly better controls and prolongs the release of drug. This is in line with the objective of this study. The result was shown in figure no. 4 and Table 7.

4.2.6 Particle size and zeta potential, PDI

4.2.6.1 Nanodispersion

The mean particle size was determined with the help of a zetasizer. The average mean particle size was calculated. The average mean diameter of D1 to D4 was analyzed. The result of optimized batch D3 show in figure no 4. In which the particle size of polymer nanoparticles is 154 nm and the Zeta potential is -16mv which indicates moderate stability of the formulation. The result shown in figure no. 5 And 6 Polydispersivity index of NE3 Batch is 0.098 which indicates monodispersity.

4.2.6.2 Pickering nanoemulsion

The size of Pickering nanoparticles was determined of all batches of formulation. The optimized batch NE3 of Pickering nanoemulsion gives the average particle size 220nm standard particle size varies from 100 -500 nm hence consider as nanoemulsion preparation. Results of optimized formulation NE3 are shown in Figure no. 6. PDI is a very crucial parameter to check particle size distribution. The monodisperse formulations have less value for PDI the optimized formulation shows PDI between 0.220 is showing monodisperse characteristics. Zeta potential is determine to check the stability of the formulation. Zeta potential is between ±40 to ±60mV having an ideal repulsive force to achieve good physical stability of the nano formulation. The zeta potential of optimized formulation NE3 was found to be -46mV indicate good stability of formulation. Results are shown in 3 Fig. 7 and 8.

| Table 1. Formulation of Nano dispersion |
| Sr. no. | Formulation batches | Ingredients (Quantity) | Eudragit | Acetone | Tween 80 | Water |
|--------|---------------------|------------------------|---------|--------|---------|-------|
| 1      | D1                  | 25gm                   |         | 20ml   | 2%      | 25ml  |
| 2      | D2                  | 20gm                   |         | 15ml   | 3%      | 30ml  |
| 3      | D3                  | 50gm                   |         | 25ml   | 1%      | 75ml  |
| 4      | D4                  | 45gm                   |         | 30ml   | 4%      | 50ml  |

| Table 2. Formulation of Pickering nanoemulsion |
| Sr. No. | Formulation Code | Ratios Aq:oil phase | Aqueous phase (nanaodispersion) (X1) | Oil phase | Captex-300 (MCT)(X2) |
|---------|------------------|---------------------|-------------------------------------|-----------|----------------------|
| 1       | NE1              | 4:1                 | 75 ml                              | 100       | 300                  |
| 2       | NE2              | 4:2                 | 75ml                               | 100       | 200                  |
| 3       | NE3              | 4:1                 | 75ml                               | 100       | 100                  |
| 4       | NE4              | 2:1                 | 50ml                               | 100       | 300                  |
| 5       | NE5              | 2:2                 | 50ml                               | 100       | 200                  |
| 6       | NE6              | 2:3                 | 50ml                               | 100       | 100                  |
| 7       | NE7              | 1:2                 | 25ml                               | 100       | 300                  |
| 8       | NE8              | 1:3                 | 25ml                               | 100       | 200                  |
| 9       | NE9              | 1:4                 | 25ml                               | 100       | 100                  |
Table 3. Solubility of Ketoprofen

| Solvent                  | Observed Solubility [16,25] (mg/ml) |
|--------------------------|-------------------------------------|
| Water                    | 0.055 mg/ml                         |
| Phosphate buffer pH 6.8  | 0.107 mg/ml                         |
| Ethanol                  | 0.109 mg/ml                         |

Table 4. Determination of PH of all Formulation batches

| Formulation code | PH measurement |
|------------------|----------------|
| NE1              | 1.2            |
| NE2              | 1.2            |
| NE3              | 6.8            |
| NE4              | 5.10           |
| NE5              | 5.15           |
| NE6              | 5.14           |
| NE7              | 5.09           |
| NE8              | 4.8            |
| NE9              | 4.9            |

Table 5. Viscosity measurement of Optimized batch NE3

| Formulation code | Torque % | RPM | Viscosity |
|------------------|----------|-----|-----------|
| NE3              | 95%      | 50  | 1143      |
|                  |          | 60  | 947       |
|                  |          | 100 | 571       |
|                  |          | 150 | 369       |

Table 6. % Drug release from Tablet formulation and premix (Captex -300+Drug)

| Time in Min | % Cumulative drug release. (Tablet) | % Cumulative drug release (Premix) |
|-------------|-------------------------------------|-----------------------------------|
| 30          | 20.40 ±0.070                        | 25.47±0.054                       |
| 60          | 40.38±0.072                         | 45.57±0.044                       |
| 90          | 60.83±0.042                         | 75.88±0.045                       |
| 120         | 78.57±0.046                         | 91.89±0.056                       |
| 150         | 88.58±0.055                         | 100                               |
| 180         | 92.78±0.073                         | -                                 |

Table 7. % drug release of optimized of Pickering nanoemulsion batch [NE 3]

| Time (min) | % cumulative drug release |
|------------|---------------------------|
| 30         | 3.84±0.045                |
| 60         | 8.16±0.043                |
| 120        | 15.45±0.051               |
| 180        | 25.54±0.057               |
| 240        | 38.59±0.038               |
| 300        | 43.54±0.039               |
| 360        | 71.85±0.042               |
| 420        | 82.18±0.047               |
| 480        | 87.57±0.038               |
| 540        | 89.51±0.051               |
| 600        | 96.93±0.054               |
4.2.7 Transmission electron microscopy

The morphological characterization of the nanoemulsion transmission electron microscopy study was performed. The TEM image shows that nanoemulsion droplets are well differentiated from each other. And conserving their shape even after vacuum establishment during TEM observation i.e. not spread on carbon support with a sample of nanoemulsion [26-28]. This means that the interface is stabilized by aggregated NPs and this particle creates a rigid film that acts as a physical barrier against Flocculation and Coalescence. Fig. 9 shows the TEM image of nanoemulsion.

4.2.8 Stability study

Stability study was done for optimized batch as per ICH guideline for novel drug delivery system. The entrapment efficiency, Zeta Potential, Particle size, was calculated. The stability study showed no change in the Entrapment Efficiency, Zeta potential, Particle size after 1, 2 and 3 time periods. The results are shown in Table 8.

Table 8. Stability study for optimized batch NE3

| Sr no | Duration of month | %entrapment efficiency | Zeta Potential | Particle size |
|-------|-------------------|------------------------|----------------|--------------|
| 1     | 1                 | 92.14±2.66%            | -46.2 mV       | 220nm        |
| 2     | 2                 | 91.89±1.45%            | -46.2 mV       | 220nm        |
| 3     | 3                 | 91.74±2.06%            | -46.1 mV       | 220nm        |

Fig. 1. a) FTIR spectra of Ketoprofen b) FTIR spectra of Eudragit RL-100, and c) FTIR spectra of mixture (Ketoprofen + Eudragit RL-100)
Fig. 2. Physical appearance of Pickering nanoemulsion (optimized batch NE3)

Fig. 3. % Drug entrapment efficiency of all batches NE1 to NE9

Fig. 4. % drug release from Marketed Tablet, Premix (Ketoprofen + Captex -300) and Optimized batch of Pickering nanoemulsion formulation NE3
Fig. 5. Particle size of nanodispersion batch D3

Fig. 6. Zeta potential of nanodispersion batch D3

Fig. 7. Particle size of Pickering nanoemulsion Batch NE3
5. CONCLUSION

From all observations and results obtained it can be concluded that all the prepared formulations show satisfied organoleptic properties. The characterization of drug and excipient was done, all results are compared with the standards and from results, it was concluded that drug and excipient are pure and of standard quality. The Particle size of the nanoparticles in nanodispersion is around 154 nm and nanoemulsion formulation is around 220 nm which showing high stability. Zeta potential of the formulation is around – 46 indicating good stability of formulation. The in-vitro drug release assessment of marketed tablet, and premix compare with optimized formulations of nanoemulsion further confirmed the use of Eudragit nanoparticles in inhibiting the release of ketoprofen for prolong period of time as well as enhanced stability of formulation. Transmission electron microscopy shows the nanoemulsion droplets are well differentiating from each other [25,29]. Finally, we have found that release of model drug was significantly slowed down when nanoemulsion is formulated by using eudragit nanoparticle, in comparison with controls. The results of the stability study shows that formulation can be stabilized by the use of eudragit nanoparticles. This study opens new prospects on the formulation of Pickering nanoemulsion.

DISCLAIMER

The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely
no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Pickering SU. CXCVI.—emulsions, J. Chem. Soc. Trans. 1907;91:2001–2021. https://doi.org/10.1039/CT9079102001.
2. Ramsden W. Separation of solids in the surface-layers of solutions and 'suspensions' (observations on surface-membranes, bubbles, emulsions, and mechanical coagulation), preliminary account, Proc. R. Soc. London., 1904;72:156–164, https://doi.org/10.1098/rspl.1903.0034.
3. Vladisavljevic GT, Shimizu M, Nakashima T, Schubert H, Nakajima M. Production of Monodispersed Emulsion Using Shirasu Porous Glass Membranes, in: Finely Dispersed Part; 2005.
4. Piacentini E, Drioli E, Giorno L. Membrane emulsification technology: Twenty-five years of inventions and research through patent survey, J. Membr. Sci. 2014;468.
5. Yuan Q, Aryanti N, Gutiérrez G, Williams RA. Enhancing the Throughput of Membrane Emulsification Techniques To Manufacture Functional Particles, Ind. Eng. Chem. Res. 2009;48.
6. Rayner M, Marku D, Eriksson M, Sjöö M, Dejmek P, Wahlgren M. Biomass-base particles for the formulation of Pickering type emulsions in food and topical applications, Colloids Surf. A Physicochem. Eng. Asp. 2014;458:48–62. https://doi.org/10.1016/j.colsurfa.2014.03.053.
7. Sonneville-Aubrun J-T, Simonnet F. L’Allorét, Nanoemulsions: A new vehicle for skincare products, Adv. Colloid Interface Sci. 2004;108–109:145–149. https://doi.org/10.1016/j.cis. www.drugbank.com
8. Habibur Rahman, Ranganathan Hariprasad. In Nanobiomaterials in Drug Delivery; 2016.
9. Piyush P, Mehta 1, Vividha S, Pawar. Electrospun nanofiber scaffolds: Technology and applications.
10. Yadav A, Chaudhari S. Formulation and characterization of Nanocochelete for 378 improvement of permeability of drug. J. Adv. Pharm. Res. 2016;16:23.
11. Particle Sciences, Emulsions and Emulsification, Tech. Brief. 2009;9.
12. Sarker M, Tomczak N, Lim S. Protein Nanocage as a pH-Switchable Pickering Emulsifier, ACS Appl. Mater. Interfaces. 2017;9.
13. Castel V, Rubiolo AC, Carrara CR. Droplet size distribution, rheological behavior and stability of corn oil emulsions stabilized by a novel hydrocolloid (Brea gum) compared with gum arabic, Food Hydrocoll. 2017;63.
14. https://www.slideshare.net/sagarsavle/Eudragit.
15. Bhure MV, Hemke AT. UV-Spectrophotometric Methods for Determination of Aceclofenac and Diclofenac in Pharmaceutical Formulation; 2010.
16. Munali R, Patel 1, Rashmin B, Patel 1, Shivam D, Thakore 2. Nanoemulsion in drug delivery Journal Pharmaceutical Developement and Technology; 2020.
17. Kaltsa O, Gatsi I, Yanniotis S, Mandala I. Influence of Ultrasonication Parameters on Physical Characteristics of Olive Oil Model Emulsions Containing Xanthan, Food Bioprocess Technol. 2014;7.
18. Sidy Mouhamed Dienga. Pickering nanoemulsions stabilized by Eudragit RL100 nanoparticles as oral drug delivery system
for poorly soluble drugs. Journal of Colloids and Surfaces B: Biointerfaces; 2020.

21. Bhure MV, Hemke AT. UV-Spectrophotometric Methods for Determination of Aceclofenac and Diacerein in Pharmaceutical Formulation; 2010.

22. Berg JM, Romoser A, Banerjee N, Zebda R, Sayes CM. The relationship between pH and zeta potential of ~30 nm metal oxide nanoparticle suspensions relevant to in vitro toxicological evaluations. Nanotoxicology. 2009;3(4):276-283.

23. Du WL, Niu SS, Xu YL, Xu ZR, Fan CL. Antibacterial activity of chitosan409 tripolyphosphate nanoparticles loaded with various metal ions. Carbohydr. Polym. 2009;75(3):385-389.

24. Manga MS, Cayre OJ, Williams RA, Biggs S, York DW. Production of solid-stabilised emulsions through rotational membrane emulsification: influence of particle adsorption kinetics, Soft Matter. 2012;8.

25. Sun G, Qi F, Wu J, Ma G, Ngai T. Preparation of Uniform Particle-Stabilized Emulsions Using SPG Membrane Emulsification, Langmuir. 2004;30.

26. Santos HM, Lodeiro C, Capelo-Martínez J-L. Ultrasound in Chemistry, 2nd ed., Wiley-VCH; 2006.

27. Nakashima T, Shimizu M, Kukizaki M. Membrane Emulsification by Microporous Glass, Key Eng. Mater. 1992;61–62.

28. Joscelyne SM, Trägardh G, Membrane emulsification—A literature review, J. Membr. Sci. 2000; 169.

29. Kelder JDH, Janssen JJM, Boom RM. Membrane emulsification with vibrating membranes: A numerical study, J. Membr. Sci. 2007;304.

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