



Journal of Applicable Chemistry

2019, 8 (4): 1776-1782
(International Peer Reviewed Journal)



Curcumin Loaded Nano-Emulgel as a Drug Carrier Having Potent Antioxidant Activity

Pankaj Dinesh Baviskar¹ and Hemant P. Narkhede^{2*}

1. Department of Chemistry, Moolji Jaitha College, Jalgaon- 425001, **INDIA**

2. Department of Chemistry, Smt. P. K. Kotecha Mahila Mahavidyalaya, Bhusawa-425201, **INDIA**

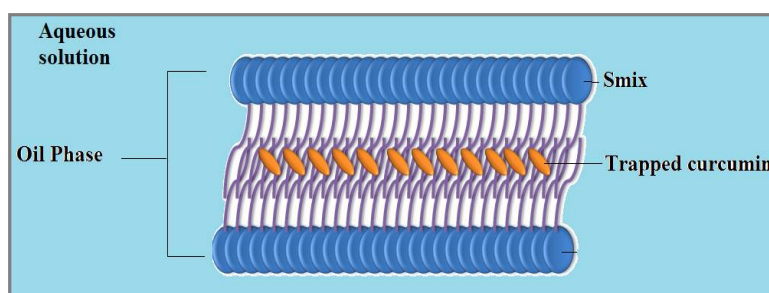
Email: pdb242424@gmail.com, narkhede.hemant@rediffmail.com

Accepted on 29th May, 2019

ABSTRACT

Curcumin has less water solubility property hence possess depressed bioavailability. Curcumin has good antioxidant activity. The enhancement in antioxidant activity of curcumin was achieved by nano-emulgel formulation of curcumin. Nanoformulation of curcumin was prepared by using sonication method. The Micelles were found to have least possible droplet size in homogeneously suspended form in nanoemulgel formulation. The nano-emulgel of curcumin was capable to disperse in water in the presence of surfactants. Chemical structure of curcumin retains after its Nanoformulation in the form its stable emulsion. The curcumin in well suspended condition in the nano size micelles shows potent antioxidant activity. The remarkable achievement of this method was improvement in antioxidant properties of curcumin.

Graphical Abstract



Keywords: Curcumin, Nano-emulsion, Nano-emulgel, Antioxidant activity.

INTRODUCTION

Curcumin is foremost ingredient of turmeric, more efficient and admirably bioactive component, found in rhizome of turmeric plant. Curcumin is naturally occurring polyphenolic compound. Curcumin is orange colored pigment extracted from curcuma longa. Curcuminoid consist of three components Curcumin, Demethoxy curcumin and Bis-demethoxy curcumin out of these three components Curcumin is in major proportion. Curcumin [(E,E)-1,7-bis (4-hydroxy-3-methoxy-phenyl)-1,6-heptadiene-3,5-ione] [**1**] (Figure 1).

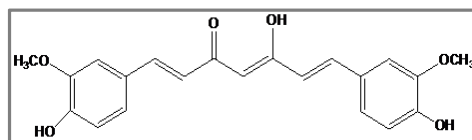


Figure 1. Curcumin.

It is naturally polyphenolic compound widely use as anti oxidant properties. However due to the fact of lower solubility property curcumin possess low bioavailability [2]. The enhancement in water solubility is achieved by emulsification of curcumin [3].

The curcumin exhibits free radical scavenging property and antioxidant property [4]. The nanoformulation of drug shows high bioavailability. High bioavailability is the measure of elevated water solubility. The nanoformulation of curcumin has potent antioxidant activity. However the effect of nano forms of curcumin in nanoemulgel form on living cell predominant over its free form [5]. Curcumin emulsions can be obtained by using surfactants like oleic acid, albumin [6]. In order to create curcumin high concentrations in water, the micelle formation are the most acceptable [6]. Most of physiological responses of living cell to curcumin as a medicinal ingredient were enhanced by its nano emulsion form by using surfactants with the help of reverse micro emulsion technique which gives micelle of curcumin [7].

MATERIALS AND METHODS

Dichloromethane (with 3% methanol) used for the synthesis of nanoemulsions was of analytical grade. Curcumin was purchased from the Sigma-Aldrich. The ultrasound device used was Ultrasonication made by Sonics & Materials INC made in U.S.A. power of 150 W and a frequency of 30 kHz. Thin-layer chromatography (TLC) analysis was performed on silica gel Silica gel on TLC plates L×W 5 cm×10 cm, with fluorescent indicator 254 nm, coated on an alumina sheet, and 3% methanol in chloroform was used as the developing solvent. Potassium ferrocyanide used for determination of antioxidant activity. Triple de-ionized water as a ionic or polar phase. Lemon oil used as a oil phase in emulsion formation, Tween-20 and Span-20 surfactants was used to form stable emulsion system, Trichloro acetic acid was used as a reference standard for antioxidant activity.

Preparation of Nano-emulgel: Preparation of nano-emulgel of Curcumin was done by forming oil in water type of emulsion. Oil in water emulsion system was used to carry curcumin in oil droplets [8]. Two nonionic surfactants were mixed in varying concentration in order to obtain appropriate HLB (hydrophilic-lipophilic balance) value of surfactant mixture [9]. The total surfactant mixture concentration also evaluated, oil phase ratio in the form of lemon oil vary in relatively narrow range (14%-18% w/w) while the aqueous phase in the form of water (80% w/w) [10]. Table 1 shows the parameters involved in the present study. The surfactants were homogenously mixed in aqueous phase, and then the organic phase in the form of lemon oil was added in to the aqueous solution [11].

Table 1. Formulation parameters used in formulation selection

Group	Lemon oil (%w/w)	Water (%w/w)	Surfactant mixture (%w/w)	Span-20 (%w/w)	Tween-20 (%w/w)	Particle size of micelle (nm)	Zeta potential (mV)
I	18	80	2.0	1.4	0.6	372.2	-11.8
II	17	80	3.0	1.8	1.2	--	--
III	16	80	4.0	2.2	1.8	--	--
IV	15	80	5.0	2.6	2.4	296.3	-8.65
V	14	80	6.0	3.0	3.0	--	--

The good emulsion system for medicinal purpose must have to lowest ratio of surfactants [12]. From above table it was observed that group I emulsion system possess lowest surfactant mixture (%w/w) hence considered as a appropriate formulation.

Loading of curcumin: The powdered curcumin solution 0.1% column purified curcumin solution Dichloromethane was added in to the centrifugal tube containing mixture of surfactant mixture and lemon oil in the appropriate ratio as describe in above section. The curcumin solution was prepared by suing DMSO as solvent. Oil phase with surfactant mixture in its appropriate concentration were added in triple distilled water (80% w/w aqueous phase). Salt increase the degree of phase separation and stability of emulsions hence 2% sodium chloride solution (1% w/w) added to the above mixture [13, 14]. The resultant loaded curcumin with emulsion system was stirred by using high-speed homogenizer at 3000 rpm for 30 min. After homogenization allow for sonication (Sonics and Materials INC made in U.S.A.) at 150W for 30 min in ice bath. The loading of curcumin is greener approach in drug modification of natural product like synthesized or modified by greener approach was done in most of the green approach reactions [15-18]. Nano material was used to modify and enhancement of properties by using nano size [19].

RESULTS AND DISCUSSION

Droplet size analysis: A scanning electron micrograph (FE-SEM) of the Nano-emulsion was recorded on a scanning electron microscope (Bruker FE-SEM analyzer,). The FE-SEM analysis shows in the figure 2 of micelles in the nanometer size. The round shape micelles were assembling in rod like structure. The average droplet size was measured about 14 nm.

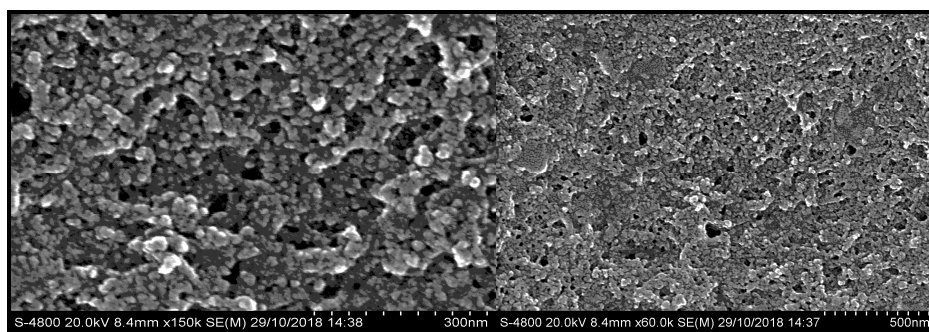


Figure 2. FE-SEM analysis of Nano-emulgel.

Energy-dispersive X-ray spectroscopy (EDX) nano-emulgel: The energy dispersive x-ray analysis (EDX) spectrum of curcumin loaded nano-emulgel is shown in figure 3. The EDX spectra indicated that the curcumin loaded nano-emulgel composed of Carbon, oxygen, and sodium in major proportion. The data confirms high purity of sample

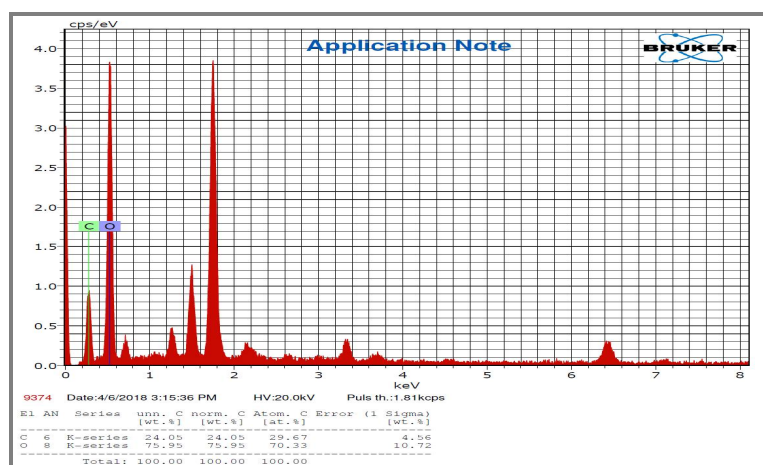


Figure 3. Energy-dispersive X-ray spectroscopy (EDX) result.

FT-IR analysis: The FT-IR analysis of curcumin and curcumin loaded nanoemulsions was measured. It was observed that the IR absorption spectra of free curcumin were somewhat different than curcumin loaded nano-emulgel. However some similar fingerprint peaks are observed but they are shifted from position. The peak at 3429.43 cm^{-1} indicates hydroxyl group in curcumin was affected in nanoemulsion and shows peak of hydroxyl group at 3386.07 cm^{-1} , the peaks at 1600-1650 for carbonyl group, peak at 1596.13 cm^{-1} for ethylene group in both curcumin and nanoemulsion of curcumin are not much affected, the peaks at 758 cm^{-1} , 833.25 cm^{-1} due to the C-H bond of alkyl group. In case of curcumin nanoemulsion these peaks were observed in the same region as shown in figure 4.

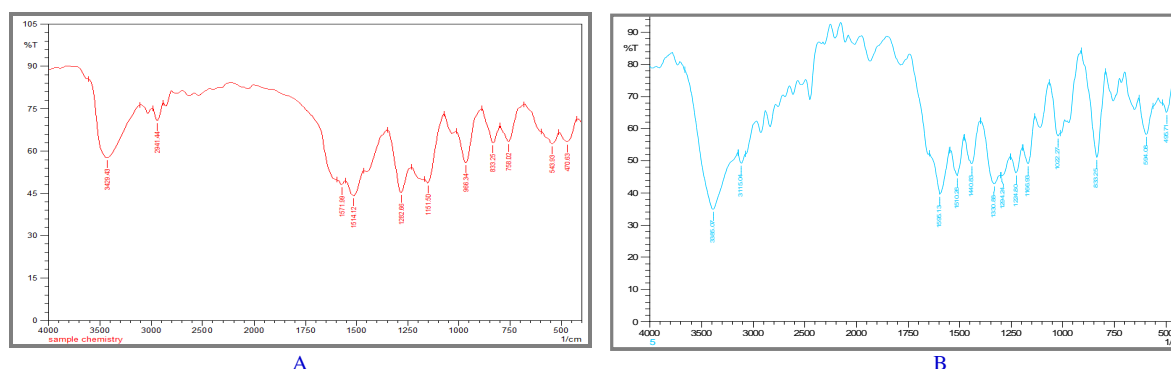


Figure 4. FT-IR spectral analysis of Curcumin and Nano-emulgel are A and B respectively.

Particle size Measurements: The particle size analysis was carried out by using particle size analyzer. Malvern particle size analyzer instrument was used for analysis of particle size of micelles. The particle size distribution of curcumin loaded gel of is totally depends on reaction conditions such as reaction time and S mix. The average size of micelles was measured and plotted in particle size analyzer statistics. However, it is evidently seen that the size of nano micelles was found to be about 372.4 nm, 296.2 nm, to as shown in figure 5.

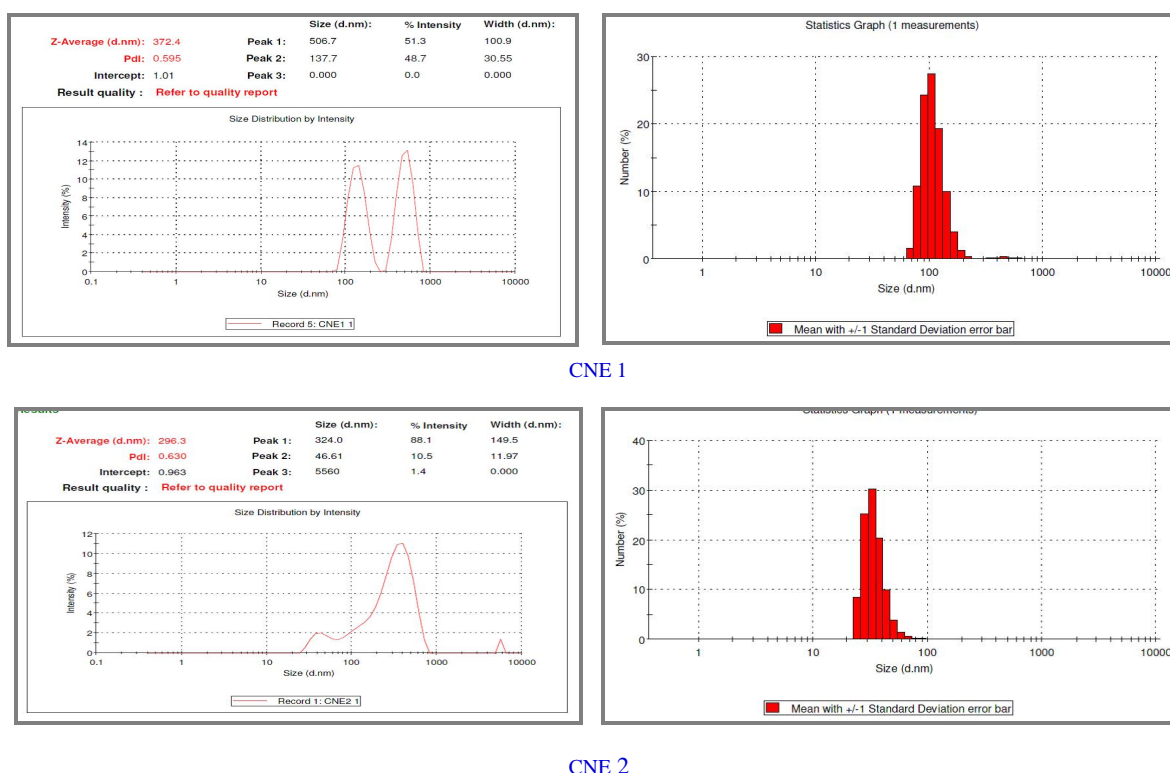


Figure 5. particle size analysis and statistical size distribution results.

Zeta potential analysis: The potential of Nano-emulgel formulation was analyzed by using an electrophoretic light scattering technique using a Malvern Zetasizer (Malvern Instruments, Ltd., UK) at wavelength 633 nm by applying 1v electric field. The nano-emulgel formulation dispersed in double distilled water (1% solution in water). The zeta potential of emulsion droplets value was found to be 14.2 mV as shown in figure 6. The zeta potential explains about stability of emulsions and surface statistics. The zeta potential of sample CNE 01 was found to be -11.8 mV and for CNE 02 was -8.65 mV

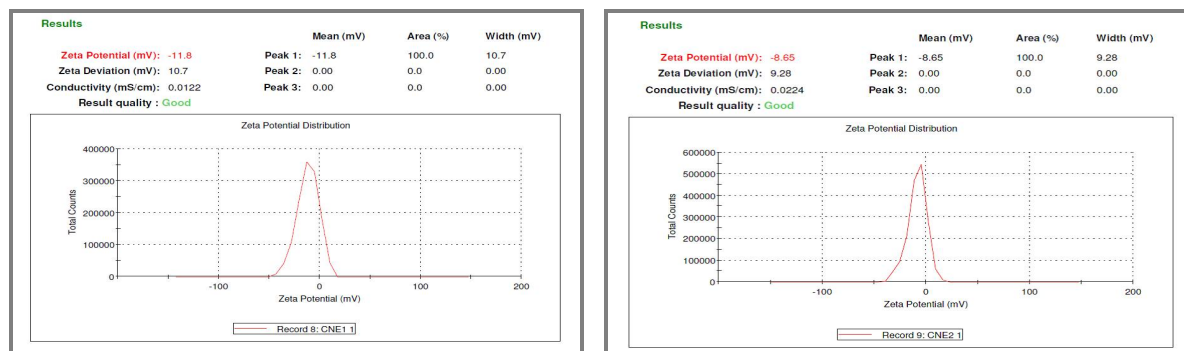


Figure 6. Zeta potential analysis result.

Antioxidant activity:

The ferric reducing anti-oxidant power (FRAP) assay: The antioxidant activity nano-emulgel of curcumin was measured with comparison of antioxidant activity of lemon oil, trichloro acetic acid and curcumin. The different concentrations curcumin loaded nanoemulgels were added in 2.5 mL of 0.2 M sodium phosphate buffer having pH 6.5 and 2.5mL of potassium ferricyanide 1 % [$K_3Fe(CN)_6$] solution. The reaction mixture was stirred well and incubated at 50°C for 30 min. at the end of the incubation 2.5 ml of 10% Trichloroacetic acid was added to the mixture and centrifuged at 3000 rpm for 15 min. After the centrifugation, supernatant 2.5 mL of solution was mixed with 2.5 mL of double distilled water and 0.5 mL of 0.1% ferric chloride solution. The colored solution was use to measure absorbance at 700 nm wavelength against the blank with reference to standard with the help of UV-Visible spectrophotometer. In the present study ascorbic acid was used as a reference standard. The antioxidant activity is measure of reducing power of the sample were comparable with reference slandered as shown in figure 8.

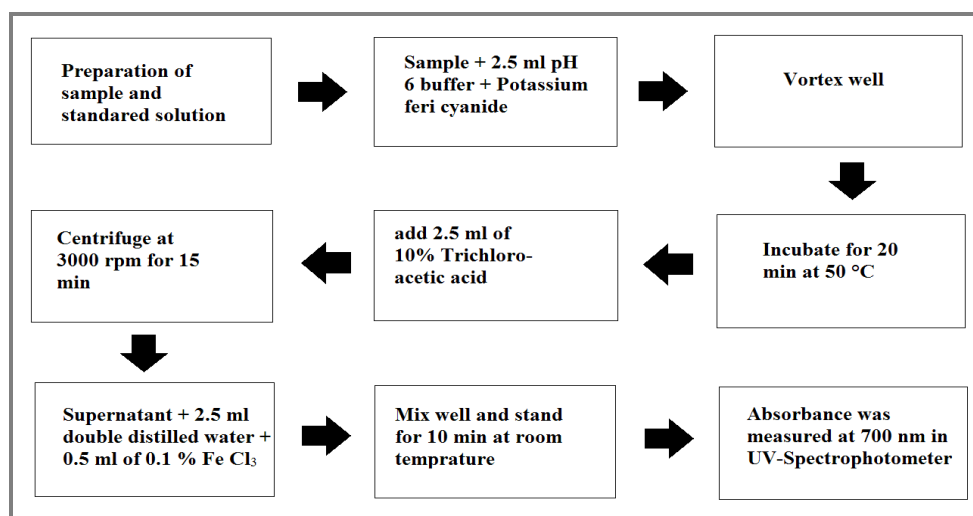


Figure 7. Flow sheet diagram of ferric reducing anti-oxidant power (FRAP) assay.

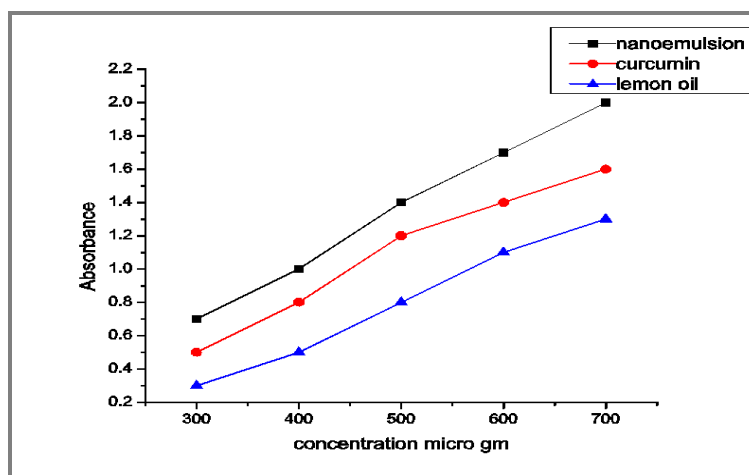


Figure 8. Antioxidant activity comparison among nanoemulsion of curcumin, curcumin and lemon oil.

APPLICATION

The uniform suspended nano micelles are great vehicles of curcumin. In the nano form curcumin can travel through micelles and reaches to target cell. The Nano form of micelles having trapped curcumin act as advanced medicine. The micelles having trapped curcumin possess more potent anti oxidant activity than its free form, the present study successfully proved that the minimum doses of drug can be maintain by using nano suspensions of micelles.

CONCLUSION

The preparation based on oil in water nano-emulsion technique. The prepared nanoemulsions gel system was having appropriate nano meter size indicated by its SEM analysis and particle size analysis while surface statistics and stability was determined by using zeta potential measurement which was found in stable range of emulsions. The nanoemulsions homogeneously distributed and have high surface area hence nanoemulsions shows strong antioxidant ability than normal curcumin. Synthesis of nano emulsion was a green synthetic approach of synthesis like most of green synthesis reactions. In the present study the nanoemulsions of curcumin formed by using lemon oil and tri chloro acetic acid TCA as an oil phase was companied with curcumin and lemon oil with respect to the reducing power (antioxidant activity) and FT-IR spectral data.

ACKNOWLEDGEMENTS

Authors are highly thankful to the University Institute of chemical technology Jalgaon, for FE-SEM, EDX, Particle size analysis and Zeta potential measurement. Authors are also thankful to Central instrumentation laboratory MooljiJaitha College Jalgaon, Smt. P. K. Kotecha MahilaMahavidyalaya Bhusawal, for providing facility of FT-IR and required chemicals respectively.

REFERENCES

- [1]. W. H. Lee, C. Y. Loo, M. Bebawy, F. Luk, R. S. Mason, R. Rohanizadeh, Curcumin and its derivatives: their application in neuropharmacology and neuroscience in the 21st century, *Current neuropharmacology*, **2013**, 11(4), 338-378.
- [2]. H. R. Rahimi, R. Nedaeinia, A. S. Shamloo, S. Nikdoust, R. K. Oskuee, Novel delivery system for natural products: Nano-curcumin formulations, *Avicenna journal of phytomedicine*, **2016**, 6(4), 383-398.

- [3]. E. Marin, M. Briceño, C. Caballero-George, Method to produce curcumin oil-in-water nanoemulsions as templates for drug carriers, *J. Biotechnol. Biomater*, **2016**, 6(247), 2-8
- [4]. T. Ak, İ. Gülçin, Antioxidant and radical scavenging properties of curcumin. *Chemico-biological interactions*, **2008**, 174(1), 27-37.
- [5]. M. Gera, N. Sharma, M. Ghosh, D. L. Huynh, S. J. Lee, T. Min, T. Kwon, D. K. Jeong, Nanoformulations of curcumin: an emerging paradigm for improved remedial application, *Oncotarget*, 2017, 8(39), 66680-66698.
- [6]. K. Priyadarsini, The chemistry of curcumin: from extraction to therapeutic agent, *Molecules*, **2014**, 19(12), 20091-20112.
- [7]. M. M. Yallapu, P. K. B. Nagesh, M. Jaggi, S. C. Chauhan, Therapeutic applications of curcumin nanoformulations, *The AAPS journal*, **2015**, 17(6), 1341-1356.
- [8]. P. Chellapa, A. T. Mohamed, E. I. Keleb, A. Elmahgoubi, A. M. Eid, Y. S. Issa, N. A. Elmarzugi, Nanoemulsion and nanoemulgel as a topical formulation, *IOSR J Pharm*, **2015**, 5, 2250-3013.
- [9]. H. T. Davis, ., Factors determining emulsion type: Hydrophile-lipophile balance and beyond. *Colloids and Surfaces A: Physicochemical and Engineering Aspects*, **1994**, 91, 9-24.
- [10]. S. Herzi, W. Essafi, Different magnesium release profiles from W/O/W emulsions based on crystallized oils, *Journal of colloid and interface science*, **2018**, 509, 178-188.
- [11]. G. P. Christy, D. A. Arimurni, M. D. P. Wahyudi, R. Martien, W. A. S. Tunjung, Formulation and Characterization of Kaffir Lime Oil Nanoemulsion, *Biosciences Biotechnology Research Asia*, **2017**, 14(3), 915-922.
- [12]. A. I. Mohamed, A. S. Sultan, I. A. Hussein, G. A. Al-Muntasheri, Influence of surfactant structure on the stability of water-in-oil emulsions under high-temperature high-salinity conditions, *Journal of Chemistry*, 2017, 28-38.
- [13]. T. Nisja, The Influence of Salts with Different Cation Valency on Oil-in-Water Emulsion Stability (Master's thesis, NTNU), **2015**.
- [14]. Y. J. Jo, Y. J. Kwon, S. G. Min, M. J. Choi, Effect of NaCl Concentration on the Emulsifying Properties of Myofibrilla Protein in the Soybean Oil and Fish Oil Emulsion, *Korean journal for food science of animal resources*, **2015**, 35(3), 315-321.
- [15]. H. P. Narkhede, P. P. Mahulikar, Microwave Induced Synthesis of Biologically Active Synthesis of N-acyloxy phthalimides Compounds. *J. Applicable Chem.*, **2015**, 4(1), 337-341.
- [16]. Jayashri D. Bhirud, H. P. Narkhede, Potassium Dihydrogen Phosphate: An Inexpensive Catalyst for the Synthesis of 2, 4, 5-Trisubstituted Imidazoles under Solvent Free Condition, *J. Applicable Chem.*, **2016**, 5(5), 1075-1079.
- [17]. H. P. Narkhede, P. P. Mahulikar, Microwave Induced Synthesis of Biologically Active Synthesis of N-acyloxy phthalimides Compounds, *J. Applicable Chem.*, **2015**, 4 (1), 337-341.
- [18]. Jayashri D. Bhirud, H. P. Narkhede, Sulfamic Acid Catalyzed One-Pot Synthesis of Biologically Relevant 4,5-dihydro-1H-pyrazole Derivatives. *J. Applicable Chem.*, **2018**, 7(5), 1166-1171.
- [19]. Yogesh. B. More, Hemant. P. Narkhede, Green Synthesis of Fe₂O₃ Nanoparticles and its Application towards Kinetic Studies on Degradation of Methyl Orange. *J. Applicable Chem.*, **2018**, 7(2), 397-402.