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Original Article

INFLUENCE OF FORMULATION FACTORS ON THE SIZE OF NANOSTRUCTURED LIPID CARRIERS AND NANOEMULSIONS PREPARED BY HIGH SHEAR HOMOGENIZATION

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ABSTRACT

Objective: The main purpose of this work was to elucidate the effect of certain formulation factors on the size of nanostructured lipid carriers (NLCs) and nanoemulsions (NEs) by using high shear homogenization method.

Methods: NLCs and NEs were prepared by high shear homogenization method using different liquid lipids types such as (Dermarol DCO® and Dermarol CCT®) at different concentrations. The effect of different concentration ratios of Tween 80 to Span 20 (2.5/1, 5/1, 10/1, 15/1) w/w % and different homogenization speeds (12 000, 18 000 rpm) on the resulted particle size were also studied.

Results: The results revealed that the optimum NLCs and NEs resulted when we use Dermarol CCT® with a concentration of 90 % as liquid lipid and decreasing surfactant ratio to (2.5/1) w/w % with increasing the homogenization speed to 18 000 rpm.

Conclusion: NLCs and NEs were successfully prepared, and from this study, it can be concluded that NLCs have the optimum particle size than Nanoemulsions.

Keywords: Nanostructured lipid carriers, Nanoemulsions, Surfactants, Liquid lipids, High Shear Homogenizer

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INTRODUCTION

In recent years, it has got to be clear that the advancement of novel medications is deficient for ensuring the advancement in medical treatment. The data obtained in the *in vitro* studies are often trailed by disappointing results in the *in vivo* or clinical circumstance. Predominant reasons for this failure are the insufficient drug level In the body due to its rapid metabolism, the high medication poisonous quality in view of broad distribution, and a high fluctuation of plasma medication levels [1].

A few methodologies have recently been explored to create nanosized drug delivery systems. These systems can be partitioned into two gatherings: polymeric and lipid systems [2]. The quantity of items in view of polymeric nanoparticles in the business sector is restricted in light of the poisonous quality of polymers, what's more, the absence of suitable expansive scale generation strategies. All together to conquer these issues, a lot of hope has been centred on lipid-based carriers, for example, nanoemulsions (NEs) and nanostructured lipid carriers (NLCs). NEs are medication conveyance systems comprising of emulsified oil and water systems with mean droplet diameters ranging from 50 to 1000 nm. Generally, the normal droplet size is somewhere around 100 and 500 nm and can exist as oil-in-water (o/w) or water-in-oil (w/o) form, where the internal phase is either oil or water, separately [3, 4]. These systems have points of interest for medication conveyance, for example, the utilization of physiologically tolerated lipids, large-scale production, prevent the medications from destruction, enhanced bioavailability, and controlled-release qualities [5]. The flaws of NEs are poor drug loading capacities, medication deterioration during storage and they have physical instability that can be increased by the joined drug [6, 7]. NLCs made out of a strong lipid matrix with a certain content of a fluid lipid are another era of lipid nanoparticles. NLCs are viewed as a more advanced era of nanoparticles, which have enhanced properties for drug loading, adjustment of the delivery profile, and stable medication during storage [8-11]. Because of the lipophilic content of the NLCs, they are considered especially helpful in the administration of lipophilic medications.

Broadly speaking, energy is normally required in emulsion formulation in light of the fact that the procedure may be non-spontaneous. The creation of nanoemulsions expenses more energy than that required to deliver macroemulsions [12].

High-energy emulsification routines make utilization of instruments that use high mechanical energy to make nanoemulsions with high kinetic energy. The mechanical instruments make serious disruptive forces which separate the oil and water stages to make Nano-sized droplets. This can be accomplished with ultrasonicators, micro fluidizer and high shear Homogenizers [13-15]. Molecule size here will rely on the type of instruments utilized and their working conditions like time and temperature alongside sample properties and compositions [16].

The objective of the present work was to study the effect of certain formulation factors on the size of NLCs and NEs in order to realize the optimum formulation factors that give the optimum particle size.

MATERIALS AND METHODS

Materials

Naterol GMS® (Glyceryl stearate) as solid lipid, Dermarol DCO® is an ester of decyl alcohol and oleic acid (Decyl Oleate), Dermarol CCT® ® is a mixed triester of glycerin and Caprylic and Capric acids (Caprylic/Capric triglyceride) as liquid lipids and Tween 80® (Polysorbate80) as-surfactant were obtained from CISME Italy s. n. c. via Marcora, Milano-Italy. Span 20® (Sorbitan monolaurate) as-surfactant, and Lecithin® (cosurfactant). All other chemicals are of HPLC grade.

Preparation of NLCs and NEs

NLCs and NEs were prepared by high shear hot homogenization method [17, 18]. Briefly, the lipid phase consisted of Naterol GMS, as solid lipid in case of NLC was melted at 80 °C and then mixed with the liquid lipid Dermarol DCO®or Dermarol CCT® and added to the Oily surfactants (Span 20 and Lecithin), or the liquid lipids Dermarol

DCO® or CCT® Dermarol CCT® in case of NE was added to the Oily surfactants (Span 20 and Lecithin). An aqueous surfactant phase consists of Tween 80 was heated up to the same temperature of the molten lipid phase. The hot surfactant solution was poured onto the hot lipid phase and homogenization was carried out at 12, 000 or 18, 000 rpm for 4 cycles (2 min with 30 s off) using high shear homogenizer (IKA T25 digital Ultra–Turrax Germany), Then leave to cool to room temperature.

Table 1: NLC prepared at 12 000 and 18 000 rpm using liquid lipid dermarol DCO® and different surfactant ratio

NLC formula code prepared at 12 000 rpm	NLC formula code prepared at 18 000 rpm	Naterol GMS (w/w%)	Dermarol DCO® (w/w%)	Tween/Span
NLC1	NLC1*	90%	10%	2.5/1
NLC2	NLC2*	80%	20%	
NLC3	NLC3*	70%	30%	
NLC4	NLC4*	60%	40%	
NLC5	NLC5*	50%	50%	
NLC6	NLC6*	40%	60%	
NLC7	NLC7*	30%	70%	
NLC8	NLC8*	20%	80%	
NLC9	NLC9*	10%	90%	
NLC1	NLC1*	90%	10%	5/1
NLC2	NLC2*	80%	20%	
NLC3	NLC3*	70%	30%	
NLC4	NLC4*	60%	40%	
NLC5	NLC5*	50%	50%	
NLC6	NLC6*	40%	60%	
NLC7	NLC7*	30%	70%	
NLC8	NLC8*	20%	80%	
NLC9	NLC9*	10%	90%	
NLC1	NLC1*	90%	10%	10/1
NLC2	NLC2*	80%	20%	
NLC3	NLC3*	70%	30%	
NLC4	NLC4*	60%	40%	
NLC5	NLC5*	50%	50%	
NLC6	NLC6*	40%	60%	
NLC7	NLC7*	30%	70%	
NLC8	NLC8*	20%	80%	
NLC9	NLC9*	10%	90%	
NLC1	NLC1*	90%	10%	15/1
NLC2	NLC2*	80%	20%	
NLC3	NLC3*	70%	30%	
NLC4	NLC4*	60%	40%	
NLC5	NLC5*	50%	50%	
NLC6	NLC6*	40%	60%	
NLC7	NLC7*	30%	70%	
NLC8	NLC8*	20%	80%	
NLC9	NLC9*	10%	90%	

Table 2: NLC formulae prepared at 12 000 and 18 000 rpm using liquid lipid Dermarol CCT® and different surfactant ratio

NLC Formula code prepared at 12 000 rpm	NLC Formula code prepared at 18 000 rpm	Naterol GMS (w/w%)	Dermarol CCT® (w/w%)	Tween/Span
NLC10	NLC10*	90%	10%	2.5/1
NLC11	NLC11*	80%	20%	
NLC12	NLC12*	70%	30%	
NLC13	NLC13*	60%	40%	
NLC14	NLC14*	50%	50%	
NLC15	NLC15*	40%	60%	
NLC16	NLC16*	30%	70%	
NLC17	NLC17*	20%	80%	
NLC18	NLC18*	10%	90%	
NLC10	NLC10*	90%	10%	5/1
NLC11	NLC11*	80%	20%	
NLC12	NLC12*	70%	30%	
NLC13	NLC13*	60%	40%	
NLC14	NLC14*	50%	50%	
NLC15	NLC15*	40%	60%	
NLC16	NLC16*	30%	70%	
NLC17	NLC17*	20%	80%	
NLC18	NLC18*	10%	90%	
NLC10	NLC10*	90%	10%	10/1
NLC11	NLC11*	80%	20%	
NLC12	NLC12*	70%	30%	
NLC13	NLC13*	60%	40%	

NLC14	NLC14*	50%	50%	
NLC15	NLC15*	40%	60%	
NLC16	NLC16*	30%	70%	
NLC17	NLC17*	20%	80%	
NLC18	NLC18*	10%	90%	
NLC10	NLC10*	90%	10%	15/1
NLC11	NLC11*	80%	20%	
NLC12	NLC12*	70%	30%	
NLC13	NLC13*	60%	40%	
NLC14	NLC14*	50%	50%	
NLC15	NLC15*	40%	60%	
NLC16	NLC16*	30%	70%	
NLC17	NLC17*	20%	80%	
NLC18	NLC18*	10%	90%	

Table3: NE formulae prepared at 12 000 and 18 000 rpm using different concentrations of liquid lipids Dermarol DCO®, Dermarol CCT® and different surfactant ratio

NE Formula code prepared at 12 000 rpm	NE Formula code prepared at 18 000 rpm	Dermarol DCO® (w/w%)	Dermarol CCT® (w/w%)	Tween/Span
NE1	NE1*	90%	10%	2.5/1
NE2	NE2*	80%	20%	
NE3	NE3*	70%	30%	
NE4	NE4*	60%	40%	
NE5	NE5*	50%	50%	
NE6	NE6*	40%	60%	
NE7	NE7*	30%	70%	
NE8	NE8*	20%	80%	
NE9	NE9*	10%	90%	
NE1	NE1*	90%	10%	5/1
NE2	NE2*	80%	20%	
NE3	NE3*	70%	30%	
NE4	NE4*	60%	40%	
NE5	NE5*	50%	50%	
NE6	NE6*	40%	60%	
NE7	NE7*	30%	70%	
NE8	NE8*	20%	80%	
NE9	NE9*	10%	90%	
NE1	NE1*	90%	10%	10/1
NE2	NE2*	80%	20%	
NE3	NE3*	70%	30%	
NE4	NE4*	60%	40%	
NE5	NE5*	50%	50%	
NE6	NE6*	40%	60%	
NE7	NE7*	30%	70%	
NE8	NE8*	20%	80%	
NE9	NE9*	10%	90%	
NE1	NE1*	90%	10%	15/1
NE2	NE2*	80%	20%	
NE3	NE3*	70%	30%	
NE4	NE4*	60%	40%	
NE5	NE5*	50%	50%	
NE6	NE6*	40%	60%	
NE7	NE7*	30%	70%	
NE8	NE8*	20%	80%	
NE9	NE9*	10%	90%	

Particle size analysis

Particle size analysis of NLC and NE were carried out using Laser diffraction particle size analyzer (LD, Master size Malvern Instruments Ltd. Worcestershire. UK) at 25 ℃. Before the analysis carried out, samples were diluted using distilled water.

RESULTS AND DISCUSSION

Preparation of NLCs and NEs

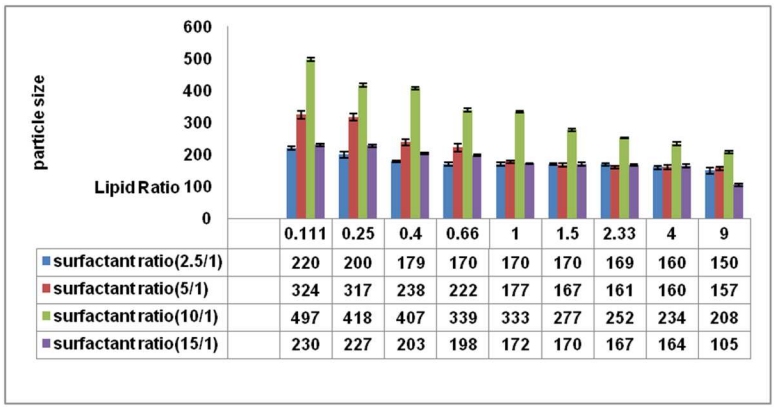
Different methods are used for the preparation of NLCs and NEs [19, 20]. In the present study, we had adopted a cost-effective, simple and reproducible method for the preparation of nanoemulsions, i.e. High shear homogenization method [17, 18].

NLCs were composed of 5(w/w %) Naterol GMS and Dermarol DCO® or Dermarol CCT® used in different concentrations and stabilized by 1(w/w %) Lecithin as co-surfactant and different ratios of surfactant concentrations Tween 80 and Span 20 (2.5/1, 5/1, 10/1, 15/1) w/w %, while NEs were composed of 5(w/w %) Dermarol DCO® and Dermarol CCT® used in different concentrations and stabilized by 1(w/w %) Lecithin as co-surfactant and different ratios of surfactant concentrations Tween 80 and Span 20 (2.5/1, 5/1, 10/1, 15/1) w/w %.

Effect of surfactants ratios on particle size

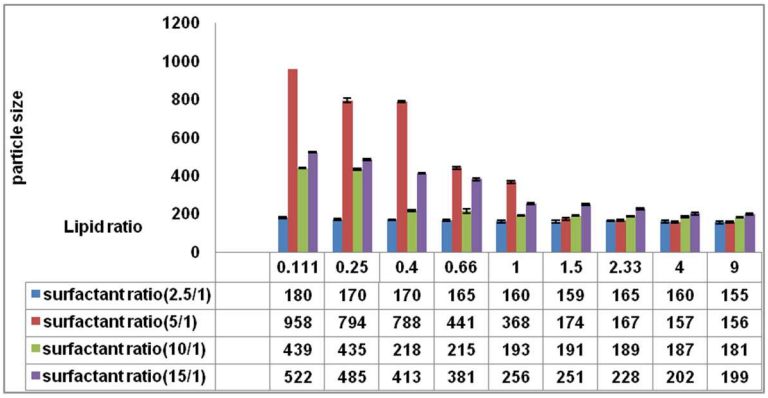
Fig. [1-12] presents the obtained results for the effect of surfactant ratio on the particle size of NEs and NLCs. firstly fig. 1, 2 demonstrate that the best NEs obtain by using the surfactant concentration ratio 2.5/1 (w/w %), While fig. 3,4 demonstrate that the best NLC obtained by using the surfactant concentration ratio (5/1), (2.5/1) w/w %. A similar results were reported by Wulff-Perez *et al.* [21] who found that at high surfactant concentrations, some surfactant molecules may

increase the local osmotic pressure, which causes moving of continuous phase between some droplets to them, and this cause depletion of the continuous phase between the drops and the aggregation happened and so the particle size increase. While different results were reported by Chanana *et al.*[22] Who found that increasing surfactant concentration leads to decrease in particle size of nanoparticles. Fig. [5-12] presents the effect of each surfactant concentration ratio on the particle size of NEs and NLCs.



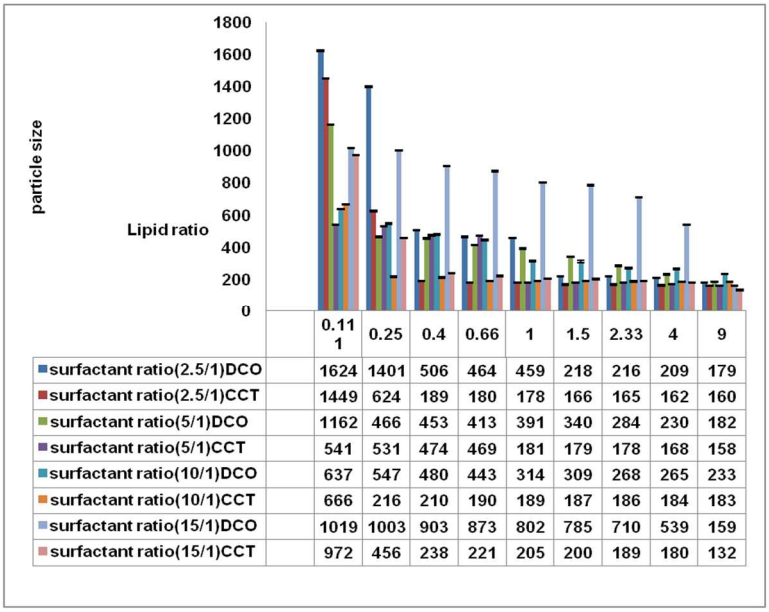
	0.111	0.25	0.4	0.66	1	1.5	2.33	4	9
surfactant ratio(2.5/1)	220	200	179	170	170	170	169	160	150
surfactant ratio(5/1)	324	317	238	222	177	167	161	160	157
surfactant ratio(10/1)	497	418	407	339	333	277	252	234	208
surfactant ratio(15/1)	230	227	203	198	172	170	167	164	105

Fig. 1: Effect of surfactant ratio on the particle size of nanoemulsions (NEs) prepared using homogenization speed at 12 000 rpm (mean±SD, N=3)



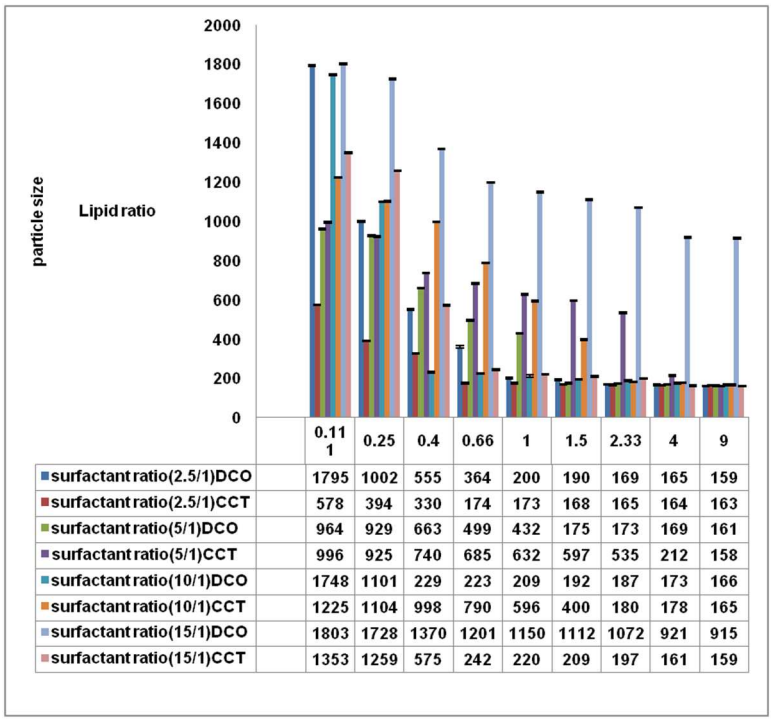
	0.111	0.25	0.4	0.66	1	1.5	2.33	4	9
surfactant ratio(2.5/1)	180	170	170	165	160	159	165	160	155
surfactant ratio(5/1)	958	794	788	441	368	174	167	157	156
surfactant ratio(10/1)	439	435	218	215	193	191	189	187	181
surfactant ratio(15/1)	522	485	413	381	256	251	228	202	199

Fig. 2: Effect of surfactant ratio on the particle size of nanoemulsions (NEs) prepared using homogenization speed at 18 000 rpm (mean±SD, N=3)



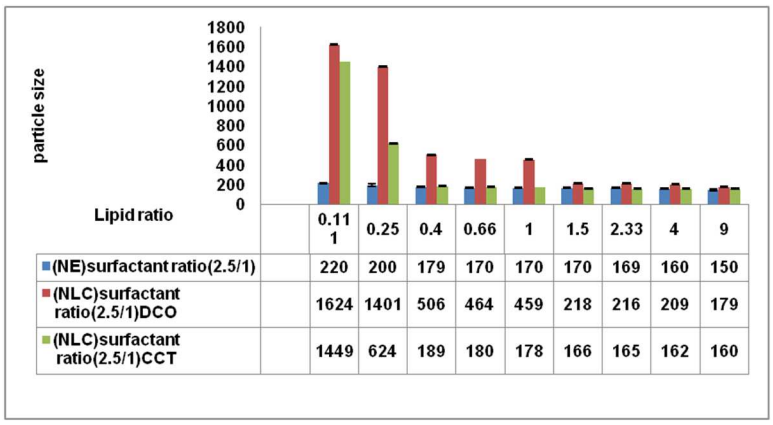
	0.111	0.25	0.4	0.66	1	1.5	2.33	4	9
surfactant ratio(2.5/1)DCO	1624	1401	506	464	459	218	216	209	179
surfactant ratio(2.5/1)CCT	1449	624	189	180	178	166	165	162	160
surfactant ratio(5/1)DCO	1162	466	453	413	391	340	284	230	182
surfactant ratio(5/1)CCT	541	531	474	469	181	179	178	168	158
surfactant ratio(10/1)DCO	637	547	480	443	314	309	268	265	233
surfactant ratio(10/1)CCT	666	216	210	190	189	187	186	184	183
surfactant ratio(15/1)DCO	1019	1003	903	873	802	785	710	539	159
surfactant ratio(15/1)CCT	972	456	238	221	205	200	189	180	132

Fig. 3: Effect of surfactant ratio on the particle size of nanostructured lipid carriers (NLCs) prepared using homogenization speed at 12 000 rpm (mean±SD, N=3)



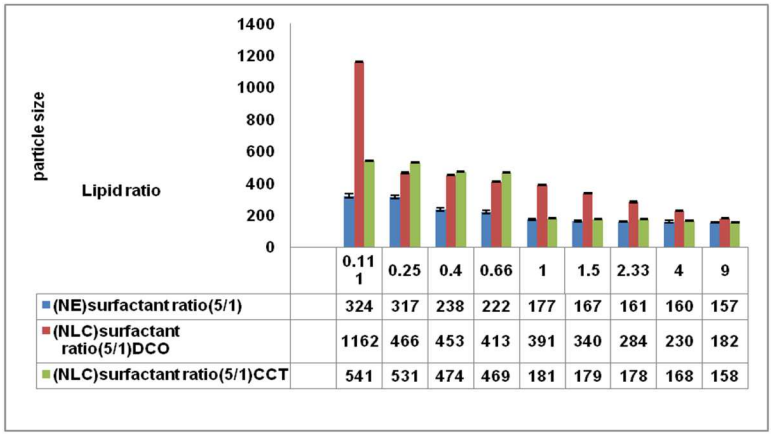
	0.11 1	0.25	0.4	0.66	1	1.5	2.33	4	9
surfactant ratio(2.5/1)DCO	1795	1002	555	364	200	190	169	165	159
surfactant ratio(2.5/1)CCT	578	394	330	174	173	168	165	164	163
surfactant ratio(5/1)DCO	964	929	663	499	432	175	173	169	161
surfactant ratio(5/1)CCT	996	925	740	685	632	597	535	212	158
surfactant ratio(10/1)DCO	1748	1101	229	223	209	192	187	173	166
surfactant ratio(10/1)CCT	1225	1104	998	790	596	400	180	178	165
surfactant ratio(15/1)DCO	1803	1728	1370	1201	1150	1112	1072	921	915
surfactant ratio(15/1)CCT	1353	1259	575	242	220	209	197	161	159

Fig. 4: Effect of surfactant ratio on the particle size of nanostructured lipid carriers (NLCs) prepared using homogenization speed at 18 000 rpm (mean±SD, N=3)



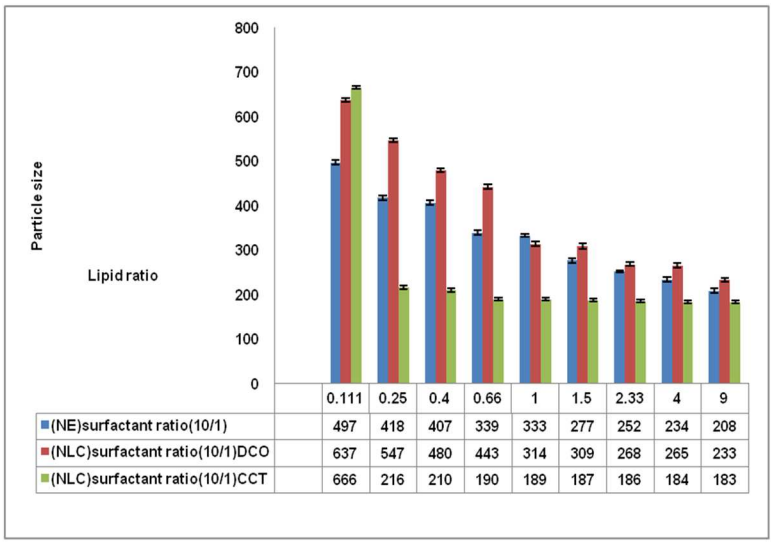
	0.11 1	0.25	0.4	0.66	1	1.5	2.33	4	9
(NE)surfactant ratio(2.5/1)	220	200	179	170	170	170	169	160	150
(NLC)surfactant ratio(2.5/1)DCO	1624	1401	506	464	459	218	216	209	179
(NLC)surfactant ratio(2.5/1)CCT	1449	624	189	180	178	166	165	162	160

Fig. 5: Effect of surfactant ratio on the particle size of nanostructured lipid carriers (NLCs) and nanoemulsions(NEs) prepared using homogenization speed at 12 000 rpm (mean±SD, N=3)



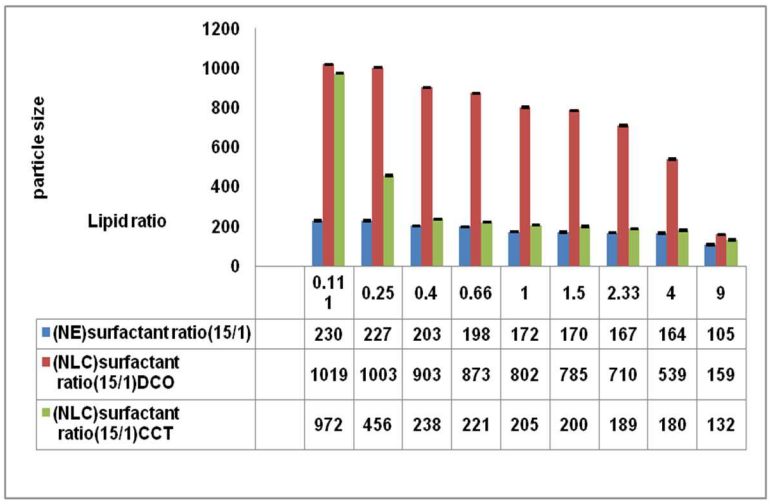
	0.11 1	0.25	0.4	0.66	1	1.5	2.33	4	9
(NE)surfactant ratio(5/1)	324	317	238	222	177	167	161	160	157
(NLC)surfactant ratio(5/1)DCO	1162	466	453	413	391	340	284	230	182
(NLC)surfactant ratio(5/1)CCT	541	531	474	469	181	179	178	168	158

Fig. 6: Effect of surfactant ratio on the particle size of nanostructured lipid carriers (NLCs) and nanoemulsions(NEs) prepared using homogenization speed at 12 000 rpm (mean±SD, N=3)



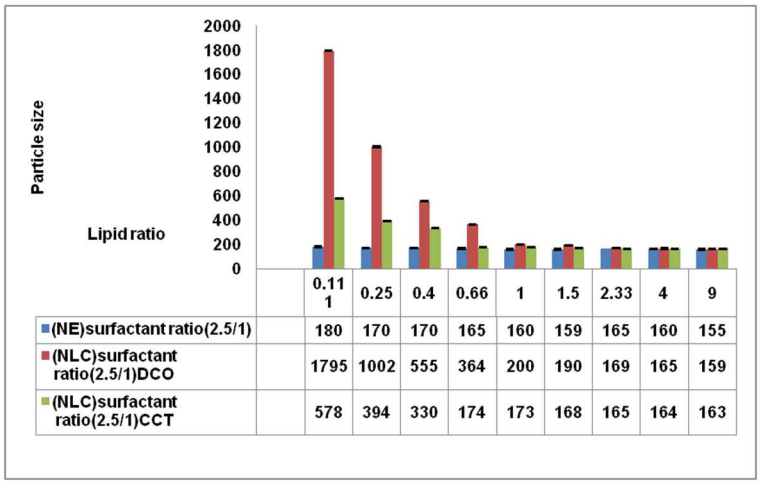
	0.111	0.25	0.4	0.66	1	1.5	2.33	4	9
(NE)surfactant ratio(10/1)	497	418	407	339	333	277	252	234	208
(NLC)surfactant ratio(10/1)DCO	637	547	480	443	314	309	268	265	233
(NLC)surfactant ratio(10/1)CCT	666	216	210	190	189	187	186	184	183

Fig. 7: Effect of surfactant ratio on the particle size of nanostructured lipid carriers (NLCs) and nanoemulsions(NEs) prepared using homogenization speed at 12 000 rpm (mean±SD, N=3)



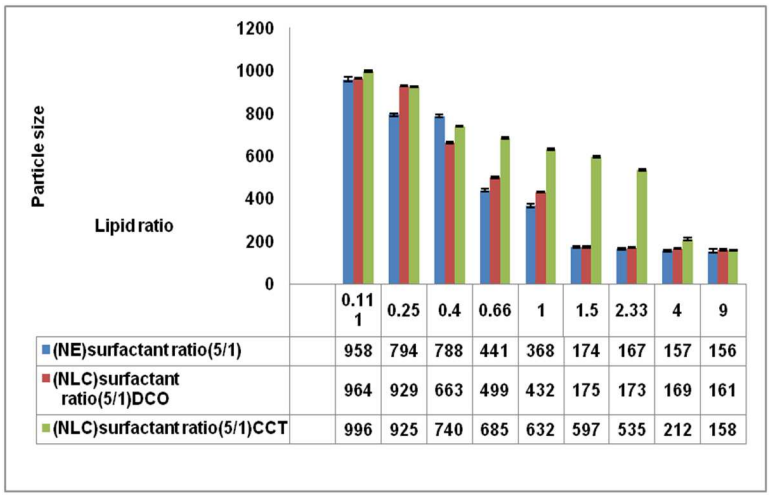
	0.111	0.25	0.4	0.66	1	1.5	2.33	4	9
(NE)surfactant ratio(15/1)	230	227	203	198	172	170	167	164	105
(NLC)surfactant ratio(15/1)DCO	1019	1003	903	873	802	785	710	539	159
(NLC)surfactant ratio(15/1)CCT	972	456	238	221	205	200	189	180	132

Fig. 8: Effect of certain surfactant ratio on the particle size of nanostructured lipid carriers (NLCs) and nanoemulsions(NEs) prepared using homogenization speed at 12 000 rpm (mean±SD, N=3)



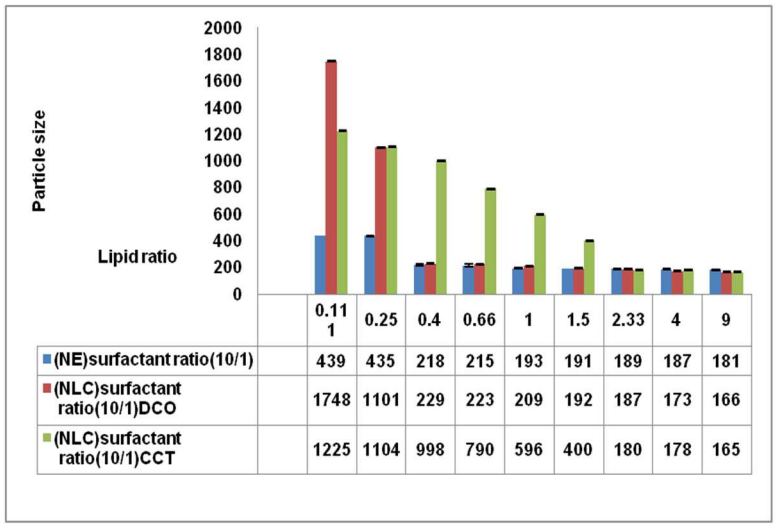
	0.111	0.25	0.4	0.66	1	1.5	2.33	4	9
(NE)surfactant ratio(2.5/1)	180	170	170	165	160	159	165	160	155
(NLC)surfactant ratio(2.5/1)DCO	1795	1002	555	364	200	190	169	165	159
(NLC)surfactant ratio(2.5/1)CCT	578	394	330	174	173	168	165	164	163

Fig. 9: Effect of certain surfactant ratio on the particle size of nanostructured lipid carriers (NLCs) and nanoemulsions(NEs) prepared using homogenization speed at 18 000 rpm (mean±SD, N=3)



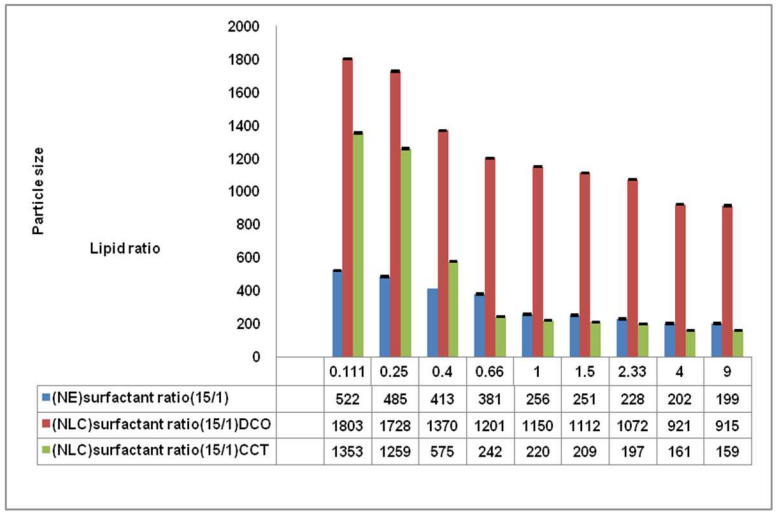
	0.111	0.25	0.4	0.66	1	1.5	2.33	4	9
(NE)surfactant ratio(5/1)	958	794	788	441	368	174	167	157	156
(NLC)surfactant ratio(5/1)DCO	964	929	663	499	432	175	173	169	161
(NLC)surfactant ratio(5/1)CCT	996	925	740	685	632	597	535	212	158

Fig. 10: Effect of certain surfactant ratio on the particle size of nanostructured lipid carriers (NLCs) and nanoemulsions(NEs) prepared using homogenization speed at 18 000 rpm (mean±SD, N=3)



	0.111	0.25	0.4	0.66	1	1.5	2.33	4	9
(NE)surfactant ratio(10/1)	439	435	218	215	193	191	189	187	181
(NLC)surfactant ratio(10/1)DCO	1748	1101	229	223	209	192	187	173	166
(NLC)surfactant ratio(10/1)CCT	1225	1104	998	790	596	400	180	178	165

Fig. 11: Effect of surfactant ratio on the particle size of nanostructured lipid carriers (NLCs) and nanoemulsions(NEs) prepared using homogenization speed at 18 000 rpm (mean±SD, N=3)



	0.111	0.25	0.4	0.66	1	1.5	2.33	4	9
(NE)surfactant ratio(15/1)	522	485	413	381	256	251	228	202	199
(NLC)surfactant ratio(15/1)DCO	1803	1728	1370	1201	1150	1112	1072	921	915
(NLC)surfactant ratio(15/1)CCT	1353	1259	575	242	220	209	197	161	159

Fig. 12: Effect of surfactant ratio on the particle size of nanostructured lipid carriers (NLCs) and nanoemulsions(NEs) prepared using homogenization speed at 18 000 rpm (mean±SD, N=3)

Effect of lipid type and concentration

Normally NEs formulate by using two liquid lipids only without solid lipid, While NLCs formulate by using solid lipid and liquid lipid, so we studied the effect of lipid concentrations on NEs particle size and the effect of lipid type and concentration on NLCs particle size. In our study, we used two liquid lipids Dermarol DCO® and Dermarol CCT® in different concentration to prepare NEs and the same liquid lipids each one separately with Naterol GMS as solid lipid to prepare NLCs.

Fig. [13–28] presents the obtained results of the effect of lipid type and concentration on the size of particles. Fig. [13,14, 16-17,19 and 20] demonstrate that NLCs prepared by using liquid lipid dermarol CCT® gave the smallest NLCs particle size, but only figs. 15 and 18 demonstrate that the best NLCs particle size resulted with Dermarol DCO® as liquid lipid, the study presents that by increasing the concentration of liquid lipid the particle size of NLCs decrease. A similar results were reported by Puglia, *et al.* and (Mu and Feng, 2003) who suggested that the addition of liquid lipid to solid lipid tends to promote the formation of small particle population, which may be due to increasing in molecular mobility of the matrix after liquid oil addition [23, 24]. Different results were reported by Soleimanian *et al.* [25] who suggested that particle size increase by increasing the liquid oil concentrations due to the more disordered crystalline structure inside the nanoparticles. Fig. [21-28] comparisons between NEs and NLCs prepared at different homogenization speed. It was found that the best NEs resulted when we increase Dermarol CCT® concentration and decrease Dermarol DCO® concentration, while the best NLCs obtained when we use Dermarol CCT® as liquid lipid.

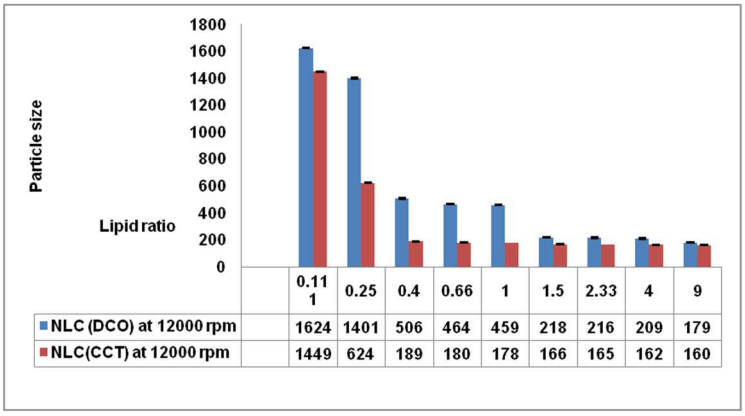


Fig. 13: Effect of lipid type and concentration on the particle size of nanostructured lipid carriers (NLCs) prepared with a surfactant ratio (2.5/1) (mean±SD, N=3)

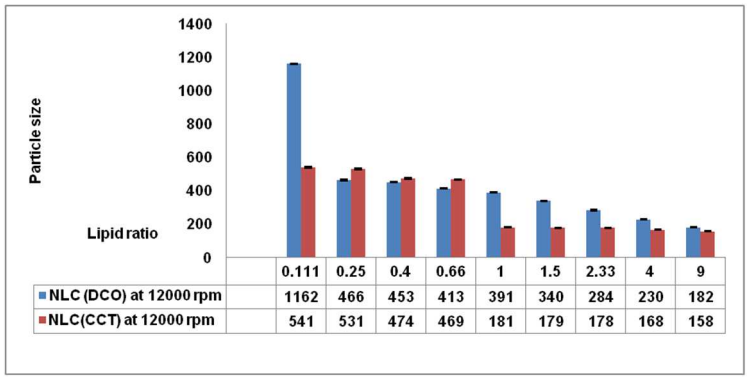


Fig. 14: Effect of lipid type and concentration on the particle size of nanostructured lipid carriers (NLCs) prepared with a surfactant ratio (5/1) (mean±SD, N=3)

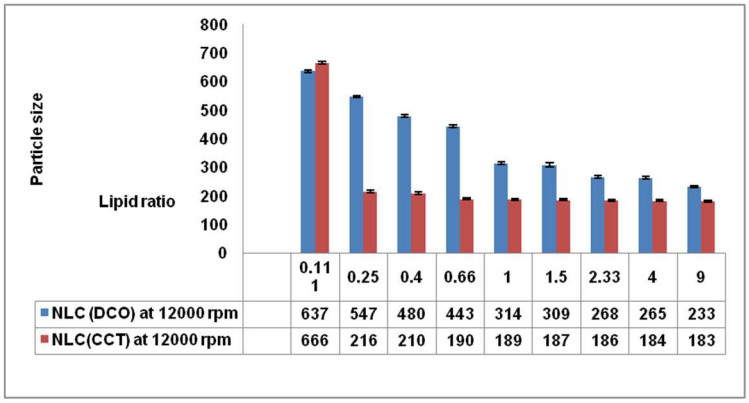
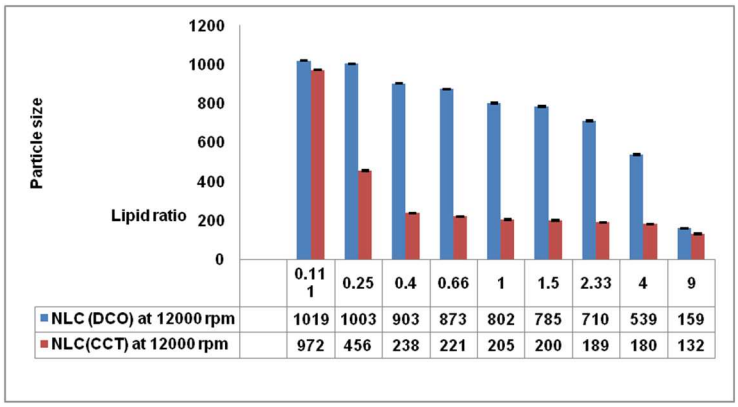
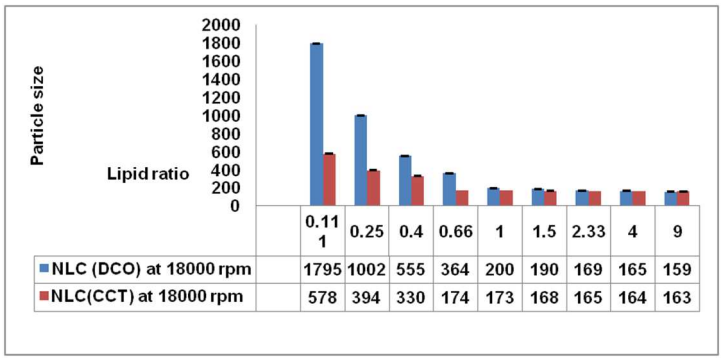


Fig. 15: Effect of lipid type and concentration on the particle size of nanostructured lipid carriers (NLCs) prepared with a surfactant ratio (10/1) (mean±SD, N=3)



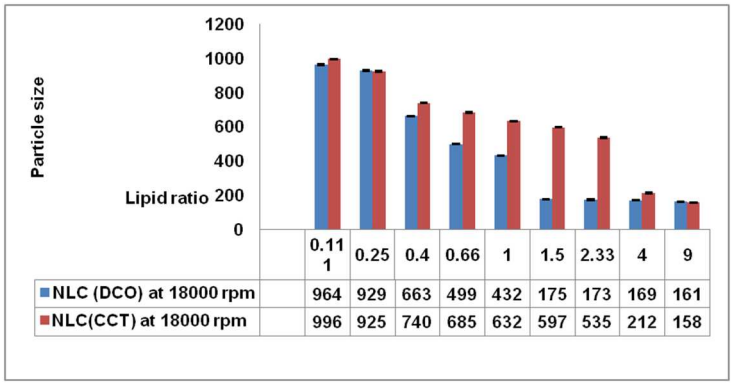
Lipid ratio	0.11 1	0.25	0.4	0.66	1	1.5	2.33	4	9
NLC (DCO) at 12000 rpm	1019	1003	903	873	802	785	710	539	159
NLC(CCT) at 12000 rpm	972	456	238	221	205	200	189	180	132

Fig. 16: Effect of lipid type and concentration on the particle size of nanostructured lipid carriers (NLCs) prepared with a surfactant ratio (15/1) (mean±SD, N=3)



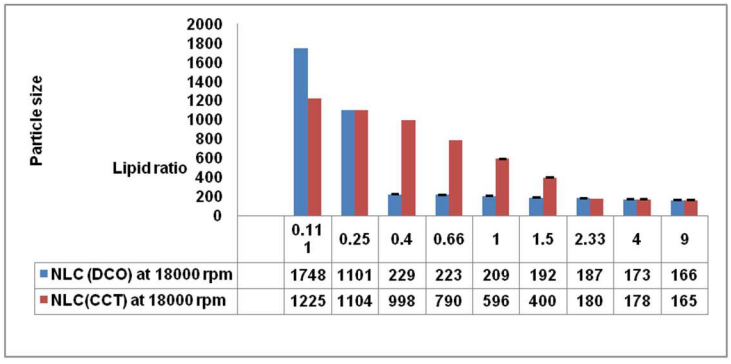
Lipid ratio	0.11 1	0.25	0.4	0.66	1	1.5	2.33	4	9
NLC (DCO) at 18000 rpm	1795	1002	555	364	200	190	169	165	159
NLC(CCT) at 18000 rpm	578	394	330	174	173	168	165	164	163

Fig. 17: Effect of lipid type and concentration on the particle size of nanostructured lipid carriers (NLCs) and prepared with a surfactant ratio (2.5/1) (mean±SD, N=3)



Lipid ratio	0.11 1	0.25	0.4	0.66	1	1.5	2.33	4	9
NLC (DCO) at 18000 rpm	964	929	663	499	432	175	173	169	161
NLC(CCT) at 18000 rpm	996	925	740	685	632	597	535	212	158

Fig. 18: Effect of lipid type and concentration on the particle size of nanostructured lipid carriers (NLCs) prepared with a surfactant ratio (5/1) (mean±SD, N=3)



Lipid ratio	0.11 1	0.25	0.4	0.66	1	1.5	2.33	4	9
NLC (DCO) at 18000 rpm	1748	1101	229	223	209	192	187	173	166
NLC(CCT) at 18000 rpm	1225	1104	998	790	596	400	180	178	165

Fig. 19: Effect of lipid type and concentration on the particle size of nanostructured lipid carriers (NLCs) prepared with a surfactant ratio (10/1) (mean±SD, N=3)

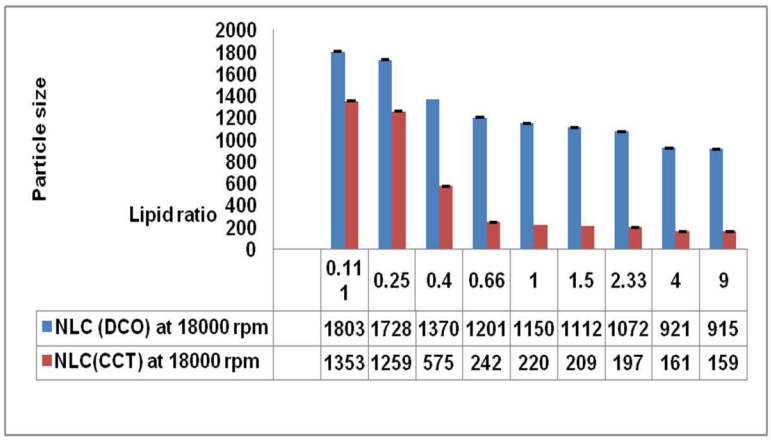


Fig. 20: Effect of lipid type and concentration on the particle size of nanostructured lipid carriers (NLCs) prepared with a surfactant ratio (15/1) (mean±SD, N=3)

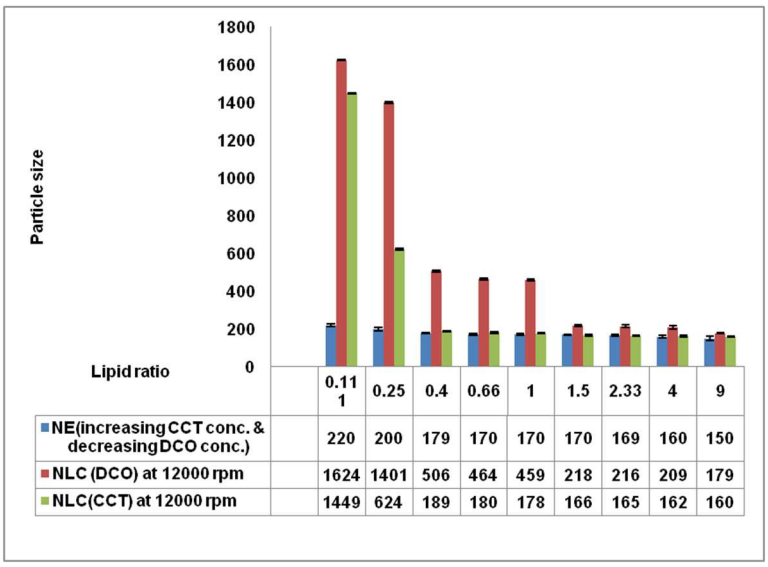


Fig. 21: Effect of lipid type and concentration on the particle size of nanostructured lipid carriers (NLCs) and nanoemulsions(NEs) prepared with a surfactant ratio (2.5/1) (mean±SD, N=3)

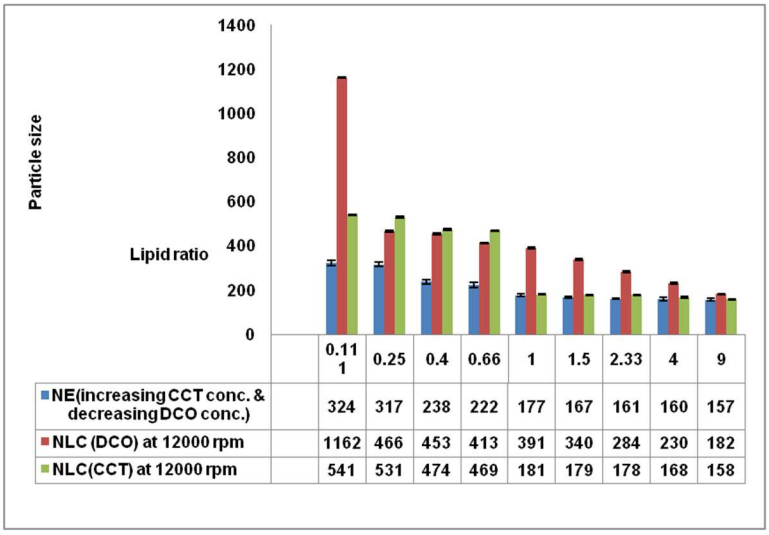
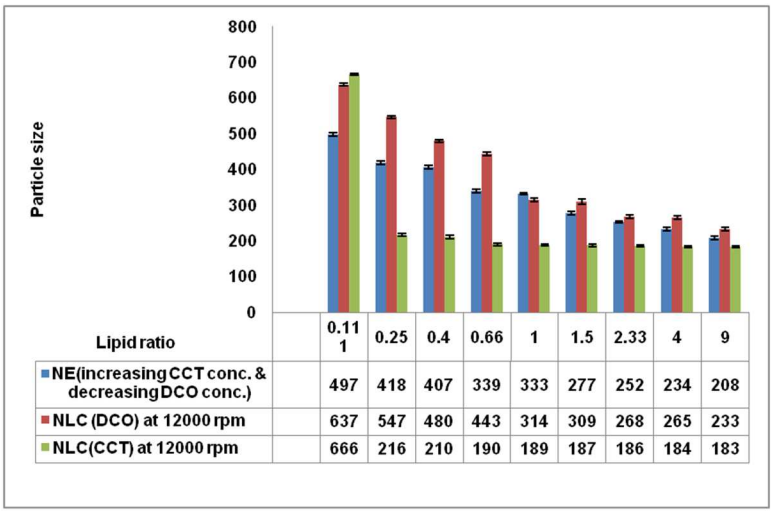
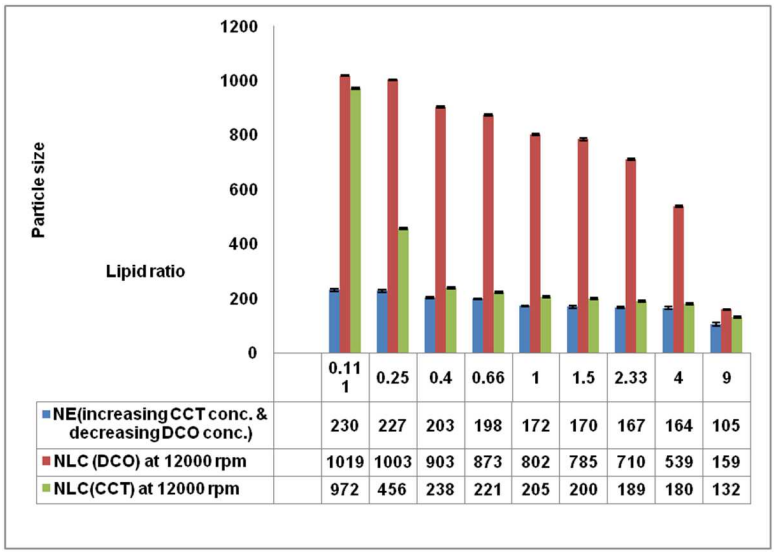


Fig. 22: Effect of lipid type and concentration on the particle size of nanostructured lipid carriers (NLCs) and nanoemulsions(NEs) prepared with a surfactant ratio (5/1) (mean±SD, N=3)



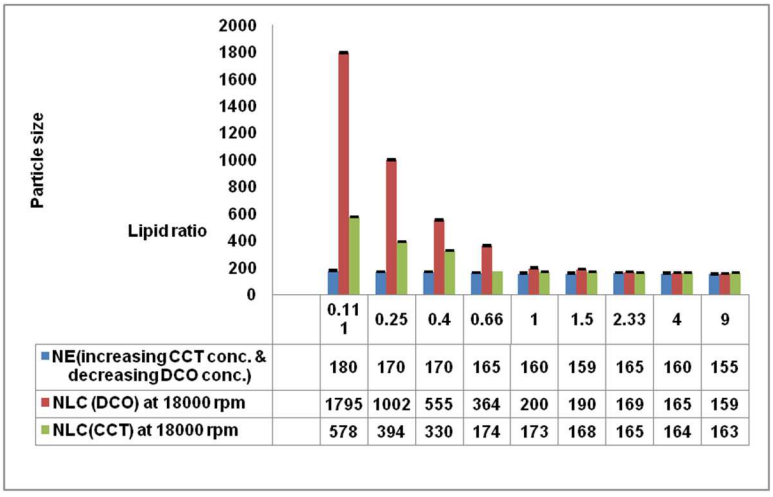
Lipid ratio	0.111	0.25	0.4	0.66	1	1.5	2.33	4	9
NE(increasing CCT conc. & decreasing DCO conc.)	497	418	407	339	333	277	252	234	208
NLC (DCO) at 12000 rpm	637	547	480	443	314	309	268	265	233
NLC(CCT) at 12000 rpm	666	216	210	190	189	187	186	184	183

Fig. 23: Effect of lipid type and concentration on the particle size of nanostructured lipid carriers (NLCs) and nanoemulsions(NEs) prepared with a surfactant ratio (10/1) (mean±SD, N=3)



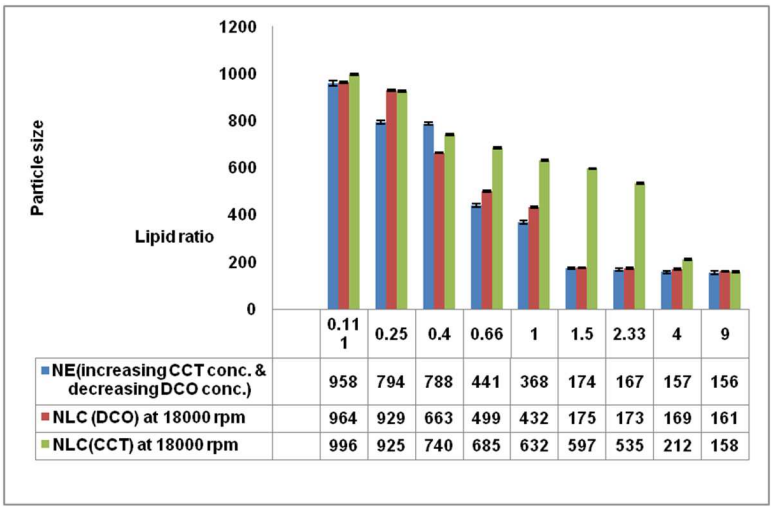
Lipid ratio	0.111	0.25	0.4	0.66	1	1.5	2.33	4	9
NE(increasing CCT conc. & decreasing DCO conc.)	230	227	203	198	172	170	167	164	105
NLC (DCO) at 12000 rpm	1019	1003	903	873	802	785	710	539	159
NLC(CCT) at 12000 rpm	972	456	238	221	205	200	189	180	132

Fig. 24: Effect of lipid type and concentration on the particle size of nanostructured lipid carriers (NLCs) and nanoemulsions(NEs) prepared with a surfactant ratio (15/1) (mean±SD, N=3)



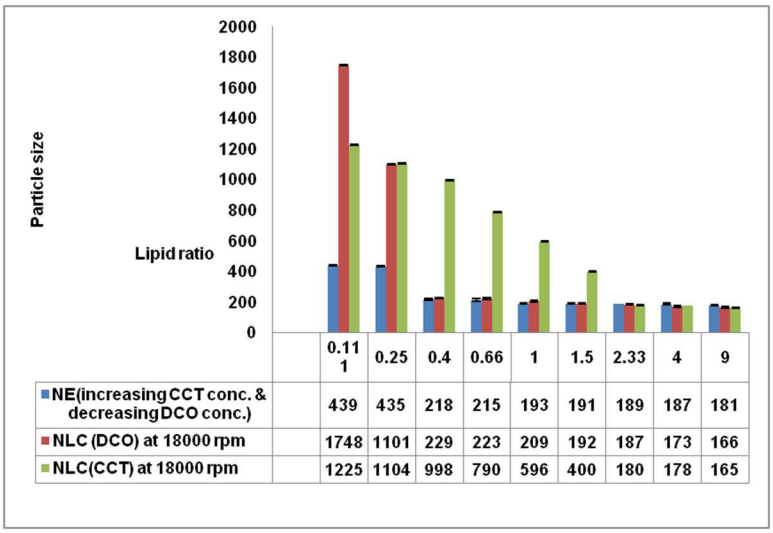
Lipid ratio	0.111	0.25	0.4	0.66	1	1.5	2.33	4	9
NE(increasing CCT conc. & decreasing DCO conc.)	180	170	170	165	160	159	165	160	155
NLC (DCO) at 18000 rpm	1795	1002	555	364	200	190	169	165	159
NLC(CCT) at 18000 rpm	578	394	330	174	173	168	165	164	163

Fig. 25: Effect of lipid type and concentration on the particle size of nanostructured lipid carriers (NLCs) and nanoemulsions(NEs) prepared with a surfactant ratio (2.5/1) (mean±SD, N=3)



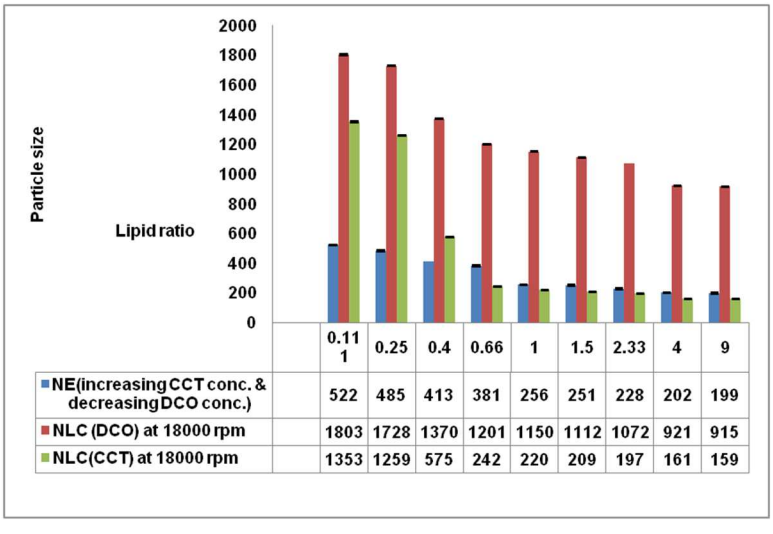
	0.11 1	0.25	0.4	0.66	1	1.5	2.33	4	9
NE(increasing CCT conc. & decreasing DCO conc.)	958	794	788	441	368	174	167	157	156
NLC (DCO) at 18000 rpm	964	929	663	499	432	175	173	169	161
NLC(CCT) at 18000 rpm	996	925	740	685	632	597	535	212	158

Fig. 26: Effect of lipid type and concentration on the particle size of nanostructured lipid carriers (NLCs) and nanoemulsions(NEs) prepared with a surfactant ratio (5/1) (mean±SD, N=3)



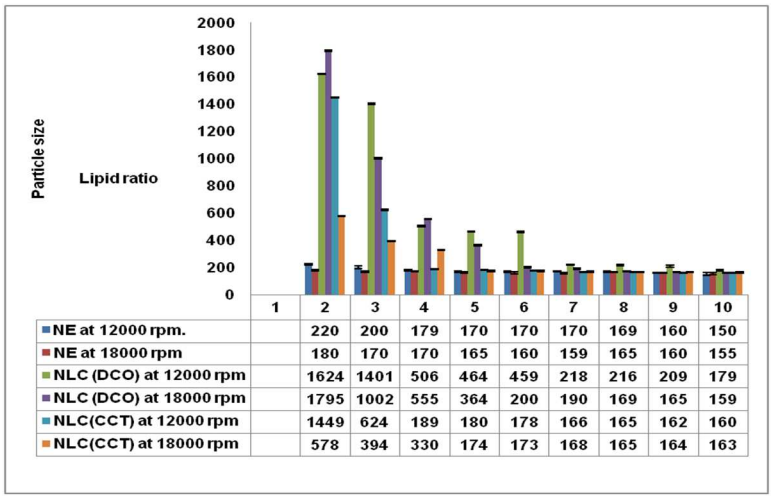
	0.11 1	0.25	0.4	0.66	1	1.5	2.33	4	9
NE(increasing CCT conc. & decreasing DCO conc.)	439	435	218	215	193	191	189	187	181
NLC (DCO) at 18000 rpm	1748	1101	229	223	209	192	187	173	166
NLC(CCT) at 18000 rpm	1225	1104	998	790	596	400	180	178	165

Fig. 27: Effect of lipid type and concentration on the particle size of nanostructured lipid carriers (NLCs) and nanoemulsions(NEs) prepared with a surfactant ratio (10/1) (mean±SD, N=3)



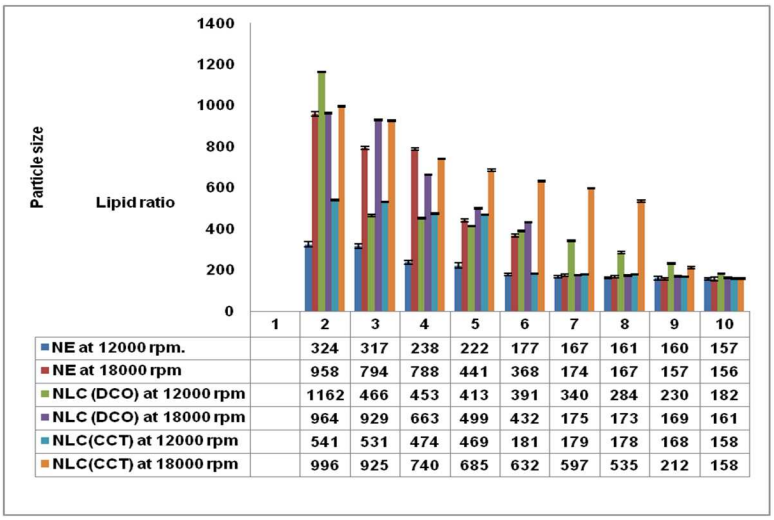
	0.11 1	0.25	0.4	0.66	1	1.5	2.33	4	9
NE(increasing CCT conc. & decreasing DCO conc.)	522	485	413	381	256	251	228	202	199
NLC (DCO) at 18000 rpm	1803	1728	1370	1201	1150	1112	1072	921	915
NLC(CCT) at 18000 rpm	1353	1259	575	242	220	209	197	161	159

Fig. 28: Effect of lipid type and concentration on the particle size of nanostructured lipid carriers (NLCs) and nanoemulsions(NEs) prepared with a surfactant ratio (15/1) (mean±SD, N=3)



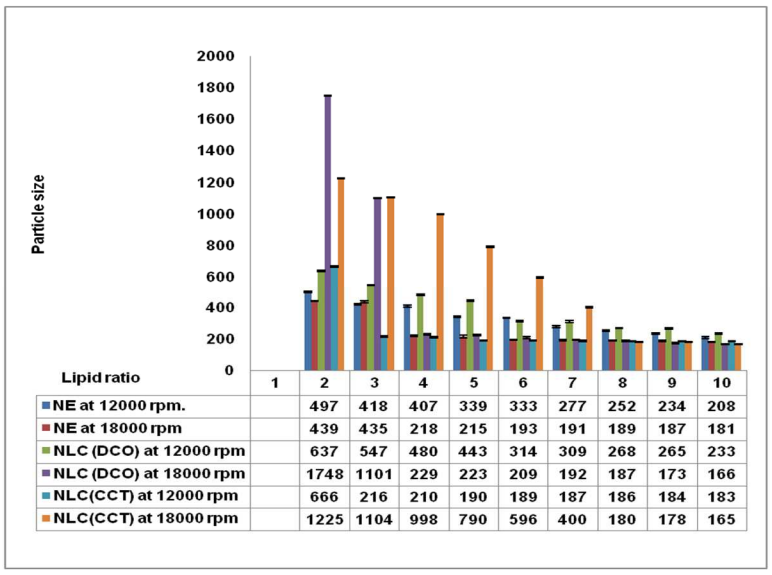
	1	2	3	4	5	6	7	8	9	10
NE at 12000 rpm.		220	200	179	170	170	170	169	160	150
NE at 18000 rpm		180	170	170	165	160	159	165	160	155
NLC (DCO) at 12000 rpm		1624	1401	506	464	459	218	216	209	179
NLC (DCO) at 18000 rpm		1795	1002	555	364	200	190	169	165	159
NLC(CCT) at 12000 rpm		1449	624	189	180	178	166	165	162	160
NLC(CCT) at 18000 rpm		578	394	330	174	173	168	165	164	163

Fig. 29: Effect of homogenization speed on the particle size of nanostructured lipid carriers (NLCs) and nanoemulsions(NEs) prepared with a surfactant ratio (2.5/1) (mean±SD, N=3)



	1	2	3	4	5	6	7	8	9	10
NE at 12000 rpm.		324	317	238	222	177	167	161	160	157
NE at 18000 rpm		958	794	788	441	368	174	167	157	156
NLC (DCO) at 12000 rpm		1162	466	453	413	391	340	284	230	182
NLC (DCO) at 18000 rpm		964	929	663	499	432	175	173	169	161
NLC(CCT) at 12000 rpm		541	531	474	469	181	179	178	168	158
NLC(CCT) at 18000 rpm		996	925	740	685	632	597	535	212	158

Fig. 30: Effect of homogenization speed on the particle size of nanostructured lipid carriers (NLCs) and nanoemulsions (NEs) prepared with a surfactant ratio (5/1) (mean±SD, N=3)



	1	2	3	4	5	6	7	8	9	10
NE at 12000 rpm.		497	418	407	339	333	277	252	234	208
NE at 18000 rpm		439	435	218	215	193	191	189	187	181
NLC (DCO) at 12000 rpm		637	547	480	443	314	309	268	265	233
NLC (DCO) at 18000 rpm		1748	1101	229	223	209	192	187	173	166
NLC(CCT) at 12000 rpm		666	216	210	190	189	187	186	184	183
NLC(CCT) at 18000 rpm		1225	1104	998	790	596	400	180	178	165

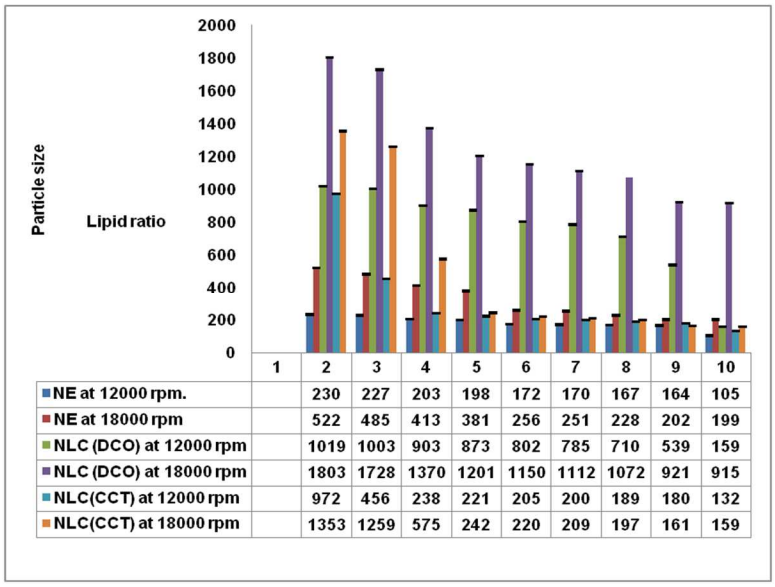
Fig. 31: Effect of homogenization speed on the particle size of nanostructured lipid carriers (NLCs) and nanoemulsions (NEs) prepared with a surfactant ratio (10/1) (mean±SD, N=3)

Effect of homogenization speed

Results of the effect of homogenization speed on the particle size of NEs and NLCs are illustrated in fig. [29–32]. This fig. reveal that increasing the homogenization speed from 12 000 to 18 000 rpm. Led to decrease the particle size of NEs and NLCs.

A similar result was obtained by Kovacevic *et al.* [26] who found that smaller particle size are obtained by increasing the homogenization speed which may be attributable to the increased force of deforming droplets at higher speed results in a decrease of particles. A different result was obtained by Lander *et al.* [27] who found that smaller particle sizes are acquired by increasing the processing temperatures because of the lowered viscosity of the lipid phase, the increase of the homogenization speed resulted in an increase of the particle size due to particle coalescence, this occurred because of the high kinetic energy of the particles. It was found that the best NEs and NLCs particle size obtained at homogenization speed 18 000 rpm.

NLCs formulated at surfactant concentration ratio 2.5/1 (w/w %) present that the mean particle size of the resulted formulations when using homogenization speed 12 000rpm ranging from 1623 nm to 179 nm while the mean particle size of the resulted formulations when using homogenization speed 18 000 rpm ranging from 1795 nm to 158 nm.



	1	2	3	4	5	6	7	8	9	10
NE at 12000 rpm.		230	227	203	198	172	170	167	164	105
NE at 18000 rpm		522	485	413	381	256	251	228	202	199
NLC (DCO) at 12000 rpm		1019	1003	903	873	802	785	710	539	159
NLC (DCO) at 18000 rpm		1803	1728	1370	1201	1150	1112	1072	921	915
NLC(CCT) at 12000 rpm		972	456	238	221	205	200	189	180	132
NLC(CCT) at 18000 rpm		1353	1259	575	242	220	209	197	161	159

Fig. 32: Effect of homogenization speed on the particle size of nanostructured lipid carriers (NLCs) and nanoemulsions(NEs) prepared with a surfactant ratio (15/1) (mean±SD, N=3)

CONCLUSION

Different formulative of factors which influenced the size of particles of NEs and NLCs prepared by high shear homogenization method were successfully studied. The results suggested the importance of controlling the critical formulation and process parameters during formulation such as (type of liquid lipids, homogenization speed, and surfactant concentration ratio) as they greatly affected the particle size of the final prepared nanoparticles. The optimum NLCs resulted when we use Dermarol CCT® as liquid lipid and surfactant ratio 2.5/1(w/w %) with homogenization speed 18 000 rpm or with a surfactant ratio 10/1 (w/w %) and homogenization speed 12 000 rpm. While the optimum NEs obtained when we increase Dermarol CCT® concentration and use surfactant ratio 2.5/1(w/w %) with homogenization speed 18 000 rpm.

AUTHORS CONTRIBUTIONS

Author Ahmed R. Gardouh designed the study, responsible of correspondence with journal and aided author Samar H. Faheim in laboratory work. All authors co-operated in writing paper, writing results, data interpretation, and reference management.

CONFLICT OF INTERESTS

Declared none

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