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Research Article

Nano emulsion of Kojic acid and Tetrahydro curcumin formulation for hyperpigmentation

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Abstract

The objective of the study was to prepare and evaluate nanoemulsion of Kojic acid and Tetrahydro curcumin formulation for hyperpigmentation using oil in water emulsion. Nanotechnology concepts are useful for damaged skin treatment. The carrier system helps to load the active ingredients to the targeted area efficiently. The nanoemulsion is a carrier system which consists of oil and water stabilized by a surfactant produced by high or low or both energy emulsification. It is considered to be the most advanced nanoparticulate system for cosmeceutical uses because it involves submicron sizes ranging from 0.020 to 0.200 um which can penetrate into deep skin cells easily. The different formulations were prepared using Kojic acid, Tetrahydro curcumin, Oliv oil, Edetate disodium, Glycerin, Sorbic acid, carbomer, Transcutol P, Glycerin, Orange essential oil and Tween 80, Purified water.The mean nanoemlsion globule size between 0.020 um-0.200 um. In vitro diffusion studies performed. Experiment 3 showed the better drug diffusion release. Experiment 3 was the optimized formulation. The Kojic acid drug diffusion release was 29.9% and Tetrahydro curcumin drug diffusion release was 29.3%. As per FDA guide lines diffusion study release should not exceed 30%. The globule size was determined by zetasizer. The stability studies were carried out foe a 90 days at 40±2°C and 75±5% RH. Stability studies indicated that Kojic acid and Tetrhydro curcumin nanoemulsion was stable.

Keywords: Kojic acid, Tetrhydro curcumin, Nanoemlsion, Homogenization, Diffusion study, Globule size.

Introduction

Hyperpigmentation is a common, usually harmless condition in which patches of skin become darker in color than the normal surrounding skin. This darkening occurs when an excess of melanin, the brown pigment that produces normal skin color, forms deposits in the skin [1]. This skin disorder may occur congenitally or inherently. Also, excessive exposure of harmful ultraviolet light and intake of certain drugs or chemicals may as well contribute to the skin condition. Kojic acid blocks tyrosinase, in turn inhibiting the production of excess pigment. Kojic acid acts as a tyrosinase inhibitor to treat overproduction of melanin in the human skin. Kojic acid can be used as an active ingredient for tyrosinase-related skin problems such as hyperpigmentation. Kojic acid can help scavenge and counteract skin-damaging free radicals caused by exposure to things such as UV damage and pollution. This not only helps improve overall skin tone as well good general anti-aging ingredient. Tetrahydro curcumin is a beta-diketone that is curcumin in which both of the double bonds have been reduced to single bonds. It has a role as a metabolite. It is a beta-diketone, a polyphenol and a diaryleptanoid. It derives from a curcumin [2].

The uniqueness of nanoemulsions that resist physical destabilization due to aggregation and gravitational separation can improve the potent activity of the nanoemulsion active ingredients. To enhance permeation of the active ingredients into the skin, an oil-in-water (O/W),trascutol P in nanoemulsion was used as a potential carrier system to be better than a water-in-oil (W/O) nanoemulsion. The composition of Kojic acid and Tetrahydrocurcumin-enriched O/W nanoemulsion and to study the interaction variables (surfactant, Oliv oil) againist response

(droplet size) [3].

Materials:

Kojic acid, Tetrahydro curcumin, Oliv oil, Edetate disodium, Glycerin, Sorbic acid, carbomer, Transcutol P, Glycerin, Orange essential oil and Tween 80, Purified water, Kojic acid, Tetrahydro curcumin, Oliv oil, Edetate Disodium, Glycerin, Sorbic acid, carbomer, Transcutol P, Glycerin, Orange essential oil and Tween 80, Purified water.

Preparation of Kojic acid and Tetrahydro curcumin O/W Nano emulsion:

The nanoemulsion was prepared using emulsification technique. The Olive oil used for better enhancement of nanoemulsion. A nonionic surfactant (Tween80) was selected to acquire better solubilization and stability of the dispersion system developed. Thus, due to its suitable HLB value, it was chosen as an O/W emulsifier. The oil phase was obtained by blending Kojic acid and Tetrahydro curcumin, while in the aqueous phase Tween80 was added to the deionized water. Both oil and aqueous phases were separately heated up to 30°C with continuous stirring using a IKA mixer to form a homogenous solution. Then, both phases were separately mixed using IKA mixer mix for 30 minutes. Using a high shear homogenizer (T25 digital ultra Turrax; IKA), the oil phase was gradually added drop wise into the aqueous phase until completion for 15 minutes at 8,000 rpm. The final mixture was further homogenized for 3 hours.

Separately Carbomer phase made using Purified water, edetate disodium dissolved in purified water under mixing. Then add carbomer in to that solution continue mixing. Then add glycerin,sorbic acid, transcutol P, and Orange oil.

Then add Kojic acid and Tetrahydro curcumin oil in water emulsion phase add to carbomer phase under mixing using IKA mixer, pH adjust to between 6.0-7.0 using 5% sodium hydroxide solution.

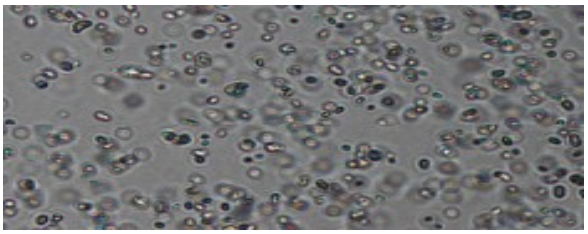
Experimental Nano formulation:

The composition of a mixture is an important aspect, Kojic acid, Tetrahydro Curcumin, Oliv oil and solubilized tween 80 deionized water on the response considered to be the droplet size. sorbic acid 0.1% (antimicrobial agents) was kept constant at 0.1%. Trascutol P 5.0% kept for formulation.Experiments conducted for correct globules formation by playing Tween 80 vs Homogenization speed.

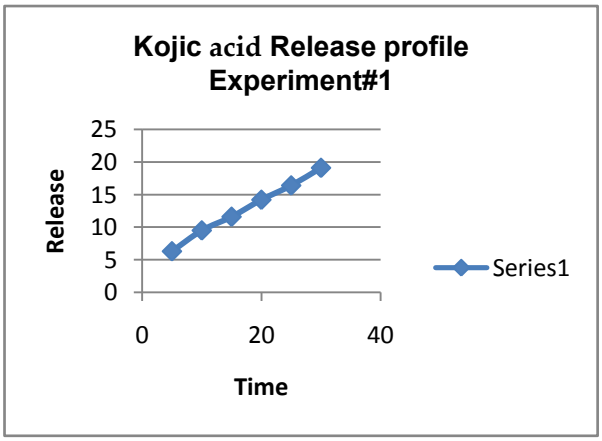
Experiment 1:

Materials	(%)
Tween 80	1
Olive oil	5
Kojic acid	1.5
Tetra hydro curcumin	0.5
Carbomer	0.5
Edetate Disodium	0.02
Glycerin	1
Sorbic acid	0.1
Transcutol P	5
Orange oil	0.2
Purified water	QS

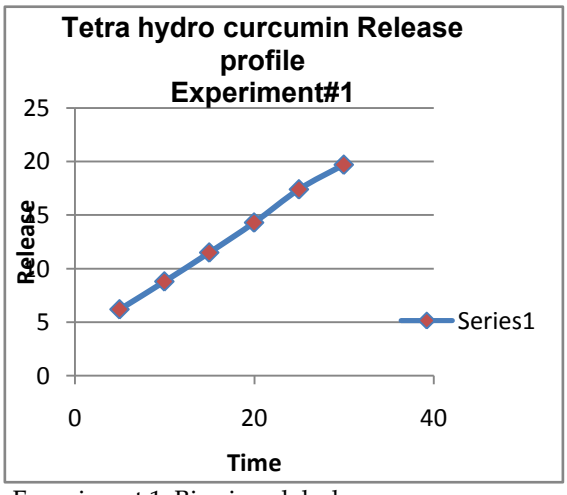
Process: Homogenization speed 5000 RPM for 3



hours



Experiment 1. Big size globules.



Experiment 1. Big size globules.

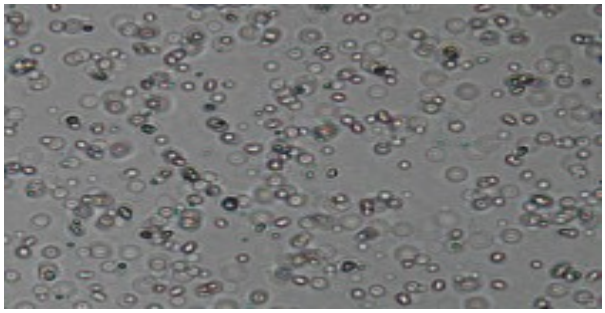
Experiment 2:

Materials	(%)
Tween 80	2
Olive oil	5
Kojic acid	1.5
Tetra hydro curcumin	0.5
Carbomer	0.5
Edetate Disodium	0.02
Glycerin	1
Sorbic acid	0.1
Transcutol P	5
Orange oil	0.2
Purified water	QS

Process: Homogenization speed 6000 RPM for 3 hours

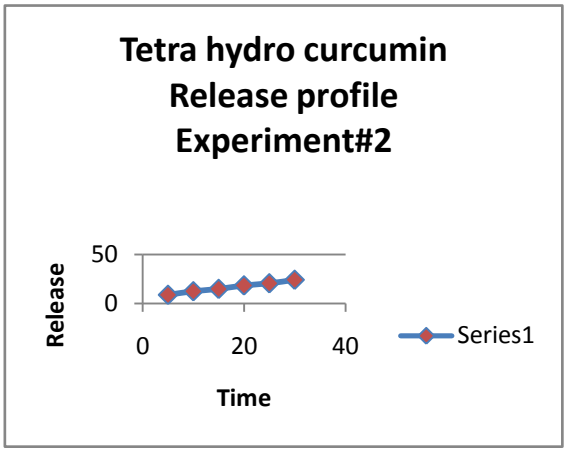
Materials	(%)
Tween 80	2
Olive oil	5
Kojic acid	1.5
Tetra hydro curcumin	0.5
Carbomer	0.5
Edetate Disodium	0.02
Glycerin	1
Sorbic acid	0.1
Transcutol P	5
Orange oil	0.2
Purified water	QS

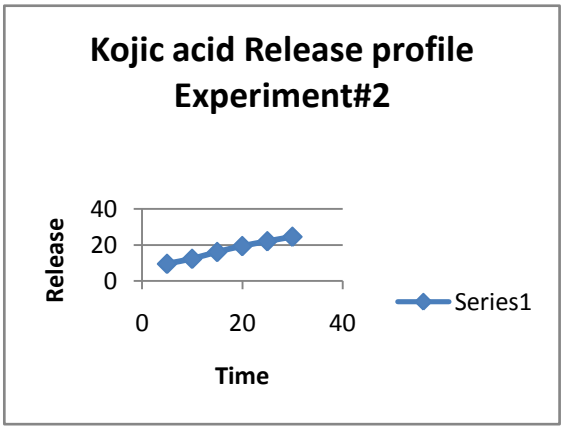
Process: Homogenization speed 6000 RPM for 3



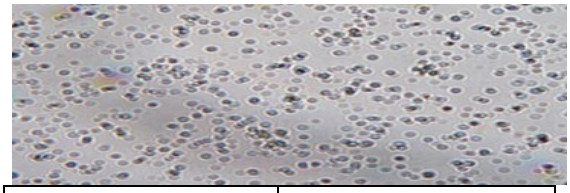
hours.

Experiment 2, Medium size globules

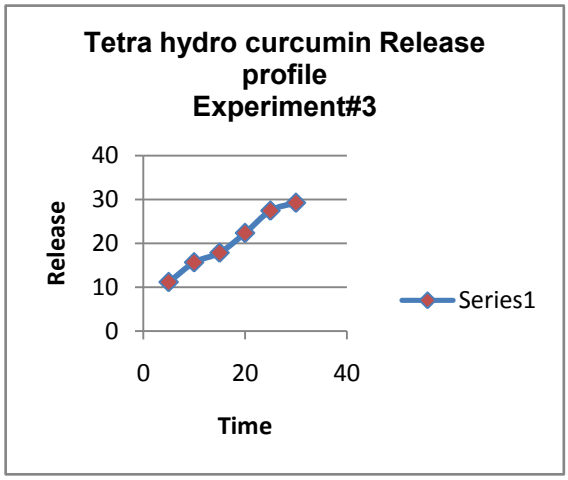


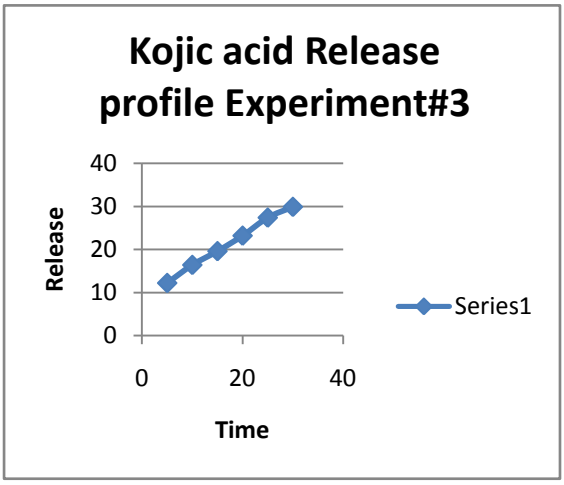


Experiment: 3

Materials	(%)
	
Tween 80	4
Olive oil	5
Kojic acid	1.5
Tetra hydro curcumin	0.5
Carbomer	0.5
Edetate Disodium	0.02
Glycerin	1
Sorbic acid	0.1
Transcutol P	5
Orange oil	0.2
Purified water	QS

Process: Homogenization speed 8000 RPM for 3 hours





Physicochemical characterization:
Dynamic light scattering method was used to measure the droplet size, stability, and size distribution of molecules in the nanoemulsions system using a droplet size analyzer (Zetasizer Nano ZS; Malvern Instruments, Malvern), scattered at an angle of 173° (temperature 25°C). The droplet size (0.020–0.200 um) was analyzed based on the intensity weighed distribution.

Globule size:

Experiment No#	D10 (um)	D50 (um)	D90 (um)
Experiment 1	0.084	0.179	0.253
Experiment 2	0.079	0.157	0.212
Experiment 3	0.072	0.110	0.179

pH Measurement:
The pH of the optimized nanoemulsion were determined using a pH meter (Mettler Toledo)

Stability studies:

Temperature and RH	Parameters	Duration in months			
		0	1	2	3
40±2°C and 75±5%	Kojic acid Assay	99.2 %	98.9 %	97.5 %	97.2 %
	Tetra-hydro curcu-min Assay	98.7 %	98.1 %	97.6 %	97.0 %

Results and discussion:
Solubility of Kojic acid and Tetrahydro curcumin in Olive oil. Vegetable oils contain many beneficial fatty acids that are widely used in cosmeceutical formulation. The therapeutic effects are well maintained when they are encapsulated in nano carrier systems. The solubility of Kojic acid and Tetrahydro curcumin in Olive oil were completely soluble.

Optimization of the responses:
The optimized formulation was developed based on the maximum amount of Kojic acid and Tetrahydrocurcumin resulting in the minimum droplet size of the nanoemulsion. Based on an optimized formulation with the composition of Kojic acid (1.5% w/w), Tetrahydro curcumin 0.5%, Tween80 (4% w/w), Carbomer (0.50% w/w), and deionized water (Q.S) was suggested wherein the nanoemulsion would have a droplet size of 0.110±0.14 um (D50) shows the response values of the optimized Kojic acid and Tetra hydro curcumin formulation. The desirability of the optimum Kojic acid and Tetra hydro curcumin formulation was 3. This showed that the quality of the formulation was agreeable and excellent.
Physicochemical characterization of optimized Kojic acid and Tetrahydro curcumin nanoemulsion

Mean droplet size:
Based on the optimized formulation, a droplet size of 0.110±0.14 um (D50). Nanoemulsions with a droplet size (D10-D90) ranging between 0.020 and 0.200 um are more favorable for cosmeceutical purpose.

pH measurement:
The pH value of the optimized formulation was 6.28±0.01.The pH values for topical preparations should be in the range of 6.0-7.0

Viscosity study:
The viscosity of the respective nanoemulsions can be determined by utilizing Brookfield cone

and plate viscometer. The Kojic acid and Tetra hydro curcumin-enriched O/W Nano emulsion viscosity was 41 cps.

Diffusion:

Conducted diffusion studies using Franz diffusion equipment with Start-M membrane (SKBMO2560).Based on the diffusion studies of experiment 1 both Kojic acid release was 19.1% and Tetrahydro curcumin release was 19.7% because of the higher globule size. Experiment 2, Kojic acid release was 24.6% and Tetrahydro curcumin release was 24.1% little more than experiment 1, because of the globule size. Experiment 3 diffusion results are promising. Experiment 3 Kojic acid release was 29.9% and Tetrahydro curcumin release was 29.3%. As per diffusion guidelines experiment 3 diffusion release was good.

Stability:

Up to 3 months accelerated stability conducted and results were promising.

Conclusion

This research indicates that an optimized composition of Kojic acid and Tetrahydrocurcumin-enriched O/W nanoemulsion is an excellent approach for topical delivery systems. The physicochemical properties of the optimized Kojic acid and Tetrahydrocurcumin-enriched O/W nanoemulsion displayed excellent diffusion results as a potential carrier for hyperpigmentation treatment.

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