Formulation development for a herbal cream incorporating the extracts of *Curcuma zedoaria* rhizome

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Abstract: *Curcuma zedoaria* is a perennial herb which belongs to the family Zingiberaceae. In traditional medicine, the rhizome of *Curcuma zedoaria* is used to treat various diseases including inflammatory conditions. The objectives of the study were to formulate a stable anti-inflammatory cream by incorporating aqueous extract of *Curcuma zedoaria* rhizome (ARE) and to investigate its phytochemicals. ARE was screened for phytochemicals. Fourteen different trial base formulations were developed by drop-wise addition of aqueous phase to the oil phase with continuous stirring at 60^0C (fusion method). The formulations were subjected to characterization tests and stability tests (real time and accelerated) for 90 days. Among them, the best two base formulations, which were stable for the tested period of 90 days, were selected. Creams with 0.75%, 1% and 1.5% (w /w) of ARE were prepared using the selected two base formulations and characterization and stability studies were conducted. Creams with 0.75% and 1% (w/w) ARE were stable for 90 days at both real and accelerated conditions. According to the characterization, all creams were identified as oil in water emulsions with pH of 6. The parent base texture was not changed after incorporating the extract. Flavonoids, tannins, alkaloids, saponins, terpenoids, carbohydrates and gums were present in ARE. It is concluded that using newly formulated bases, stable anti-inflammatory cream can be formulated by incorporating ARE of *Curcuma zedoaria*, a plant which is well known to have anti-inflammatory activity in traditional medicine. It is recommended to establish quality control standards for the novel formulation for future studies.

Keywords: *Curcuma zedoaria*, formulation, cream, stability

Introduction:

Inflammation is a protective response against harmful agents. But, the unregulated inflammation can cause harmful conditions such as life-threatening hypersensitivity reactions, cardiovascular diseases, neurogenerative diseases, cancer, *etc* (Kumar *et al*., 2005). Many currently used drugs to suppress such unregulated inflammatory activity have less curability and more side effects (Okin and Medzhitov., 2012). So, there is a huge interest in developing anti-inflammatory drugs having better efficacy and fewer side effects. Natural plant extracts are rich in many active constituents and give considerably fewer side effects. Therefore, they can be considered as possible candidates for preparing such novel drugs with better efficacy and lesser side effects (Okin and Medzhitov., 2012). *Curcuma zedoaria* belongs to the genus Curcuma Linn of the

family Zingiberaceae and it is a perennial herb which is identified to have anti-inflammatory, antinociceptive, anti-tumor, antimicrobial, analgesic and wound healing activity (Add reference). In traditional medicines, *Curcuma zedoaria* is used to treat various diseases such as inflammation, wounds, pain, skin ailments, menstrual irregularities, malaria fever,*etc.* (Ullah*et al*., 2014). The objectives of this study were to develop a stable anti-inflammatory cream by incorporating the extracts of *Curcuma zedoaria* rhizome and to investigate its phytochemicals.

Methodology:

Sample collection and authentication

The fresh rhizomes from the mature plant of *Curcuma zedoaria* were collected from Kegalle District (Coordinates: 7015'11" N 80020'43" E), Sabaragamuwa Province, Sri Lanka in June 2019. The collected plant parts were identified and their authenticity was confirmed by national herbarium, Royal Botanic Gardens, Peradeniya, Sri Lanka.

Preparation of aqueous extract of the rhizome

Fresh powdered rhizomes of *Curcuma zedoaria* (100.0 g) were boiled with 1500 mL of distilled water and the resulting filtrate was evaporated using a rotary vacuum evaporator. The resulting sludge was dried and **a**queous extract of the rhizome (ARE) was obtained.

Phytochemical analysis

The extract was screened qualitatively for the presence of alkaloids, tannins, flavonoids, saponins, terpenoids, carbohydrates and gums using standard methods of analysis described in Vishnoi (1979) and Sofowara (1993).

Preparation, stability evaluation and characterization of the base formulations.

A set of fourteen bases (S1 -S14) were prepared using different ratios of white soft paraffin, Eucalyptus oil, water, surfactants (polyethylene glycol, Tween 80), emulsifying wax, hard paraffin, liquid paraffin and stearic acid by fusion method. In fusion method, the required weight of distilled water was taken to a dry beaker and heated up to 60^0C using a water bath. At the same time, components of the oil phase including emulsifying agents were weighed to another container and heated up to 60^0C using a water bath. When components of both aqueous and oil phases were dissolved at 60^0C, the aqueous phase was added drop wise to the mixture of oil phase with continuous stirring. The prepared bases were transferred into universal bottles and centrifuge tubes and labeled accordingly.

Base formulations were subjected to real time and accelerated stability testings over a period of 3 months and observations were made on 1st, 3rd ,5th, 10th, 15th, 29th ,45th ,60th ,75th and 90th day at specific storage conditions [8 °C (in refrigerator), 25 °C, 40 °C (in oven)]. In addition, base formulations were subjected to centrifugation stability test.

In characterization, microscopic analysis, measuring pH, organoleptic evaluation and evaluation of homogenicity were performed.

Incorporation of ARE to base formulations and of preparation, stability evaluation and characterization of cream formulations

Creams with 1%, 0.75% and 1.5% (w/w) ARE of *Curcuma zedoaria* were formulated with the best two stable base formulations (S5 and S13) as mentioned in Table 1. Initially the aqueous phase was prepared by mixing the required weight of the powder of the aqueous extract with required quantity of distilled water and

heated to 60^0C sing a water bath. The components of the oil phase were weighed in to another container and heated up to the same temperature (60^0C) using a water bath. Then, the mixture of oil phase was added drop wise to the aqueous phase with continuous stirring.

The prepared creams were cooled to room temperature with continuous stirring and transferred into universal bottles and centrifuge tubes and labeled accordingly.

Results and Discussion:

Nature and yield of the extracts and phytochemical analysis

ARE of *Curcuma zedoaria* was dry, reddish powder with a characteristic odour and the percentage yield was 7.3%(w/w). Phytochemical study showed that flavonoids, tannins, alkaloids, saponins, terpenoids, carbohydrates and gums were present in ARE.

Table 1. Visual stability observations of S5, S6, S11, S12 and S13

Day	Stability of the base														
	8⁰C					RT					40⁰C				
	S5	S6	S11	S12	S13	S5	S6	S11	S12	S13	S5	S6	S11	S12	S13
1	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S
3	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S
5	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S
10	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S
15	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S
29	S	S	S	S	S	S	S	S	S	S	S	S	P	S	S
45	S	S	S	S	S	S	S	S	S	S	S	P	P	S	S
60	S	S	S	S	S	S	S	S	S	S	S	P	P	P	S
75	S	S	S	S	S	S	S	S	S	S	S	P	P	P	S
90	S	S	S	S	S	S	S	S	S	S	S	P	P	P	S

(S=Stable P= Not stable)

Stability evaluation of trial bases

S5 and S13 bases were stable at all specific storage conditions (8°C, 25 °C and 40°C) and showed no phase separation after centrifugation for all 90-day time period. The stability study of the best five formulas is given in Table 1.

Characterization of trial bases

Microscopic observations revealed that the formulated creams as oil in water emulsions. Initial pH of the creams was 6. All the trial base formulations had moderately fine texture except S5 which has very fine texture.

According to the results of above stability tests and characterization tests, S5 and S13 bases were selected as best base formulations and they were used to develop cream incorporating the plant extract.

Stability evaluation of cream

Creams formulated incorporating 0.75% and, 1.0%(w/w) of ARE of *Curcuma zedoaria* to base formulations of S5 and S13 were stable at all specific storage conditions (8°C, 25 °C and 40°C) and showed no phase separation after centrifugation for all 90-day time period (Table 2).

Table 2. Visual stability observations of cream series

Day	Temperature																	
	8⁰C						RT						40⁰C					
	S5			S13			S5			S13			S5			S13		
	0.75%	1%	1.5%	0.75%	1%	1.5%	0.75%	1%	1.5%	0.75%	1%	1.5%	0.75%	1%	1.5%	0.75%	1%	1.5%
1	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S
3	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S
5	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S
10	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S
15	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S
29	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S
45	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	P
60	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	P
75	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	P
90	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	P

(S=Stable P= Not stable)

The creams formulated incorporating 1.5%(w/w) of ARE of S5 were s *Curcuma zedoaria* table at all temperatures. However, the creams formulated incorporating 1.5%(w/w) ARE to S13 were stable only at 8°C and 25 °C.

Characterization of cream

Microscopic observations revealed that the formulated creams as oil in water emulsions. Initial pH of creams was 6. The parent base texture was not changed after incorporating the extract.

According to results and observations, S5 base is more compatible with ARE than S13 base. Also, S5 base in which white soft paraffin used as oil phase is more cost effective than S13 base in which eucalyptus oil used. Both S5 and S13 creams can be improved by incorporating anti-oxidant agents, antimicrobial agents and preservatives.

Resulting cream can be further subjected to anti-inflammatory and quality control studies to produce a marketable drug that serves as an anti-inflammatory cream.

Conclusion:

Stable anti-inflammatory cream can be formulated using newly found base formulations incorporating ARE of *Curcuma zedoaria.*

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