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PREPARATION AND EVALUATION OF *CORDIA MYXA* FRUIT TOPICAL CREAM

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ABSTRACT

Background: Use of medicinal plants is an important part of traditional medicine. One of these plants which is anciently used for its benefit properties in Iran and some other countries, is *Cordia myxa*. Because of its mucilage content, the plant fruits have been used as expectorant and emollient in treatment of cough and some respiratory problems. Based on some reports about its anti-inflammatory effect, it was aimed to prepare a topical formulation, preferably cream, and evaluate its physicochemical properties. **Objectives:** The aim of this study was to prepare topical cream containing *Cordia myxa* fruits using different bases and emulsifiers and evaluate them at in-vitro condition to achieve the best formulation. **Materials and Methods:** The fruits were provided from market, washed and extracted by distilled water. 8 formulations containing 5% of aqueous extract of *Cordia myxa* fruits and different amounts of lipids and surfactants were prepared by fusion method. Some physicochemical properties of formulations such as pH, consistency, viscosity, and physical stability, were evaluated. Antimicrobial challenge test against *Pseudomonas aeruginosa* was also carried out. **Results:** All of the formulations were homogeneous with an odor and color related to *Cordia* extract, showed a proper consistency, a pH average of 7.175 and average of 9010 cps for viscosity. They were physically stable and there was no coalescence or creaming after 1, 3, and 6 months of storage. No sedimentation and phase separation were observed after centrifugation at 2000 rpm and no microbial growth was seen after the period of storage. **Conclusions:** Regarding increasing public interest to herbal medicine applications, it should be more considered to formulate and prepare new dosage forms containing herbal medicines. *Cordia*

myxa is a plant with many useful pharmacological effects such as ant-inflammatory effect and our findings showed that it may be formulated as a topical cream.

KEYWORDS: *Cordia myxa* fruits extract, medicinal plants, topical cream, physicochemical properties.

1. INTRODUCTION

The majority of the world's population relies on the traditional medicine and major role of the traditional medicine including the use of plant extract and their active constituents.[1,2] In Iran, medicinal plants have been widely used for treatment of diseases in folk medicine. Nowadays, the herbal medicines have attracted interests of scientists and physicians due to irrational use of therapies and synthetic drugs leading to health hazards.[3]

The genus *Cordia* belongs to the family Boraginaceae, with Approximately 300 species distributed worldwide, mostly in the warmer regions of the World.[1] According to a literature survey, several uses in traditional medicine have been reported for different *Cordia* species.[4] The fruits contain protein, lipid, fibre and carbohydrates. The fruits also have high energy values and it has medicinal value as well as physiological activity due to presence of some minerals such as K, Na, Ca, Fe, and Zn.[5] Numerous natural substances existing in *Cordia* species have demonstrated promising roles in treatment and management of various forms of cancer, diabetes, degenerative disorder, and ulcerative colitis. They have activities of antimicrobial and antifungal, analgesic, antibacterial and cytotoxic, anthelmintic, gastroprotective and antiulcer, anti-inflammatory, anti-implantation, and wound healing.[1,6]
The fruit of *C. myxa* (natural order: Boraginaceae, synonym: *Cordia abyssinica*), has been used for the treatment of infections of urinary tract, diseases of the lung and spleen, and as an astringent, anthelminthic, diuretic, and demulcent agent.[7] Because of its mucilage content, the plant fruits have been used as expectorant and emollient in treatment of cough and some respiratory problems.[8] It has been reported that leaf extracts of certain species of *Cordia* such as *C. myxa*, *C. francisci*, and *C. serratifolia* have significant analgesic, anti-inflammatory, and anti-arthritic activity in the rat.[7]

Skin, the largest organ and covering of the body, is a protective barrier against different threatening microorganisms, chemicals, and harmful UV radiation. Applying drugs topically on the skin instead of orally can provides many advantages such as avoiding first pass effect, decreasing systemic administered dose, diminished side effects, and so on. This is more

important when a local drug action is desired.[9] The aim of this study was to prepare a topical product preferably cream containing *C. myxa* fruit extract and evaluate its physicochemical properties. This study could be a plan to assess anti-inflammatory effect of *C. myxa* fruit cream in ex-vivo and in-vivo conditions.

2. MATERIALS AND METHODS

2.1. Materials: The fruits were provided from the market. Stearic acid, sodium lauryl sulfate, cetyl alcohol, borax, spermaceti, triethanolamine, propyl and methyl parabene were all provided from merk (Germany). Lanolin, glycerin, and white bees wax were supplied from Sepidaj Company in Iran. Freshly distilled water was used to extract fruits and wherever required.

2.2. Methods

2.2.1. Extracting

The fruits were supplied from the Ahvaz market in Iran. After recognition, they were carefully cleaned to remove the dirt and extra genus material, washed, dried in shade, and finally powdered by grinding. Maceration in boiling water was used to extract the powder according to traditional use. To do this, 10g of the powder was macerated in 200 ml boiling distilled water for 20 mins. The macerate was first filtered through fine-woven cloth and then centrifuged at 3500 rpm for 15 mins. The supernatant was removed by evaporation until obtaining dry powder. For preparing formulations, the dried powder extract was used.[10]

2.2.2. Preparing Formulations containing extract

To prepare base creams, different amounts of ingredients were used. Table 1 shows components and their amounts used for each formulation.

Table 1. Compositions of formulations (%w/w)

Formulation	Oil Phase					Emulsifier			Aqueous Phase				
	Beea Wax (%)	Spermaceti (%)	Lanolin (%)	Stearic Acid (%)	Cetyl Alcohol (%)	Triethanolamine (%)	Sodium Lauryl Sulfate (%)	Borax (%)	Methyl Paraben (%)	Propyl Paraben (%)	Glycerin (%)	Extract (%)	Distilled Water up to
1	20	4	4	8	4	2	-	2	0.25	0.25	5	5	100
2	20	4	4	8	4	1	-	1	0.25	0.25	5	5	100
3	20	4	4	8	4	-	2	2	0.25	0.25	5	5	100

4	20	4	4	8	4	-	1	1	0.25	0.25	5	5	100
5	10	2	2	4	2	2	-	2	0.25	0.25	5	5	100
6	10	2	2	4	2	1	-	1	0.25	0.25	5	5	100
7	10	2	2	4	2	-	2	2	0.25	0.25	5	5	100
8	10	2	2	4	2	-	1	1	0.25	0.25	5	5	100

For each formulation, the amounts of components were accurately weighed using analytical balance (METLER TOLIDO, Switzerland), each phase prepared separately on bathroom (Memmert, Germany) with maximum temperature of 70° C, and finally the aqueous phase was gradually added on oil phase containing emulsifier at the same temperature. The mixture was stirred continuously till forming emulsion. The amount of extract used in all formulations was constant of 5%.

2.2.3 Evaluation of formulations

2.2.3.1 Organoleptic properties

The appearance, odor and color of the creams were visually evaluated. These parameters were assessed by at least 3 persons to avoid any bias effect.

2.2.3.2 Microscopic Homogeneity

Consistency, presence of turbidity, and instability of formulations were also microscopically evaluated via an optical microscope (Olympus, Model CHS, Japan) using lenses with magnification of 10x and 40x.[11]

2.2.3.3 Physical stability

Any change in color or odor and any sign of breaking, creaming, coalescence, or bleeding of cream from the container during (within 1 week and 1 month) or after storing at room temperature for three months, were considered as physical instabilities.[11]

2.2.3.4 Centrifugation test

The centrifugation tests were performed at 25°C and 2000 rpm for 5, 15, 30 and 60 min by puting a 10g of each formulation in a centrifuge tube having 1 cm diameter (MPW, Poland). The samples were then evaluated regarding any phase separation and/or solid sedimentation.[11]

2.2.3.5 Viscosity

Viscosity of all formulations were measured at room temperature using Brookfield viscometer

instrument (Model DV-II, USA) and spindle 34 at four different speeds after 48 hours, 1 month and 3 months from preparation. Every measurement was triplicate and average of the results calculated and used to compare formulations.[9]

2.2.3.6 pH

0.5 g of each formulation was diluted with distilled water to 50 ml and then pH was determined using a pH meter instrument (Mettler Toledo, Switzerland) immediately, 1 week, 1 month, and 3 months after preparation. Each determination repeated 3 times to generate an average pH value.[9]

2.2.3.7 Antimicrobial Preservative Effectiveness Test

To study the effectiveness and sufficiency of the preservative in the formulations, the single microbial challenge test against *Pseudomonas aeruginosa* was carried out according to procedure mentioned in USP30 for non-sterile topical products. 0.1 ml of 108 cfu/ml of the test strains, were added to 20ml pre- diluted sample of the formulations in sterile containers and incubated at 22.5±2.5 °C for 28 days. At appropriate time intervals according to the USP procedure (1, 7, 14, 21, and 28 days), 1 ml of each incubated sample was added to a plate. After incubation for 48h, the viable colony-forming units (cfu) were counted. The number of cfu in each plate and changes in microbial numbers were recorded.[11]

2.2.4. Statistical Methods for Analyzing Data

To assess the results of the study, both measurable and immeasurable findings were recorded. For statistical analysis of the results, measurable parameters were selected and their mean and standard deviation were calculated. The data were analyzed using Paired T Test and ANOVA when required and the p value was considered up to 0.05 for significance of results. Excel (Microsoft 2010) and Minitab (Ver. 14) soft-wares were used to plot figures and calculate p value and deduce the relationship between variables and responses.

3 RESULTS

3.1 Organoleptic properties and microscopic homogeneity

All formulations were homogenous and relatively similar in appearance, color, and odor. The color of creams was light brown due to nature and appearance of *Cordia* extract. Their odor was characteristic related to *C. myxa* extract. These mean that the ingredients and their amounts have not affected on organoleptic properties and appearance of formulations

significantly. Consistency of formulations was reasonable and no cloudy texture was seen in microscopic evaluation.

3.2 Physical stability

Any bleeding from the container could be a sign of breaking of emulsion and phase separation in creams. No breaking, creaming, coalescence, or bleeding were seen during or after storage at room temperature. The odor and color of formulations were also the same as freshly prepared creams. These indicate that the ingredients and their amounts in formulations had been properly selected. This is more important about emulsifying materials used in formulations.

3.3 Centrifugation test

Centrifugation at a short period of time represents a condition similar to sedimentation due to gravity in a long time or shelf life.[12] The samples all were stable during and after centrifugation indicating that creams had been sufficiently emulsified and homogenized when prepared.

3.4 Viscosity

The results of viscosity for all formulations are presented in Table 2.

Analysis of results showed a direct relationship between amount of oil phase and viscosity measured 48 h after preparing (p value 0.038 for 50 rpm as selected speed). In other words; the more percentage of oil phase, the more viscosity. This relationship has repeatedly been confirmed by other researchers such as Juntawong S. et al.[13] There were no significant correlations between emulsifier type (p value 0.99) and percentage (p value 0.444) and viscosity, so the viscosity of creams was independent of type and amount of emulsifier. Besides, changes in viscosities after 3 months was also studied and analyzed. Based on this analysis, changes in viscosity of formulations were not significant (p value 0.504).

Table 2. Viscosity of formulations at four speeds and 3 different times (mean±sd, n=3)

Formulation	Speed (rpm)	48 hours	1 month	3 months
1	10	6096±81	6182±87	6158±85
	20	4621±129	4702±143	4704±132
	50	5030±162	5169±187	5184±171
	100	3694±156	3779±167	3824±169
2	10	14125±270	14122±265	14138±254
	20	14116±252	14113±234	14157±243
	50	7959±146	7956±156	7984±149
	100	5264±156	5279±145	5312±157
3	10	10547±187	10545±195	10397±190
	20	13548±145	13545±176	13261±159
	50	5613±161	5611±124	5610±156
	100	4283±112	4279±123	4211±118
4	10	15597±231	15792±213	15752±223
	20	9568±123	9597±114	9884±119
	50	6731±89	6796±92	6789±90
	100	4271±67	4311±56	4398±63
5	10	5422±121	5399±117	5475±114
	20	4396±98	4379±101	4384±99
	50	2975±49	2986±56	2997±49
	100	1684±34	1692±41	1697±39
6	10	6683±118	6689±98	6698±101
	20	4654±87	4659±78	4714±95
	50	3797±57	3811±56	3825±67
	100	2764±89	2769±82	2790±87
7	10	8873±145	8912±132	8896±143
	20	6209±231	6265±181	6279±199
	50	4836±153	4212±145	4240±151
	100	4625±123	4695±112	4710±118
8	10	4734±112	4752±125	4772±121
	20	2784±56	2790±77	2813±69
	50	2963±58	2978±66	2810±62
	100	2048±39	2061±43	2089±54

3.5 pH

The average of pH of formulations at different times are presented in Table 3. As seen, the formulations offered a pH average of 7.175 immediately after preparation. This is a little higher than natural pH of the skin likely due to presence of triethanolamine and borax. Data obtained from analysis of regression confirmed the effect of these materials as a significant correlation (p value 0.021). However, with modifying the amount of triethanolamine and the other ingredients can reach a pH closer to natural quantity of the skin. Furthermore, although the average of pH of formulations increased after 3 months, this change was not significant (p value 0.056).

Table 3. pH of formulations at 4 different times (mean±SD, n=3)

Formulation	After Preparing	1 Week	1 month	3 months
1	7.2±0.20	7.3±0.18	7.3±0.22	7.7±0.22
2	7.2±0.22	7.4±0.23	7.6±0.27	7.9±0.24
3	7.0±o.19	7.2±o.15	7.5±o.29	7.6±o.28
4	6.7±0.17	6.9±0.19	7.2±0.27	7.4±0.27
5	7.7±0.28	7.9±0.31	7.8±0.28	7.4±0.31
6	7.4±0.26	7.5±0.29	7.6±0.27	7.9±0.27
7	7.4±0.24	6.9±0.20	7.1±0.26	7.2±0.24
8	6.8±0.16	6.5±0.19	6.8±0.19	6.9±0.18

3.6 Antimicrobial Preservative Effectiveness Test

No microbial growth in infected samples was seen after storage time. Therefore, it was shown that the antimicrobial preservatives used were able to protect the formulations against bacteria.

4 CONCLUSION

Cordia myxa is a world spread medicinal plant which has many pharmacological properties. It is commonly used for some dermatological conditions such as skin inflammation. To avoid systemic effects due to oral administration of extract in traditional medicine, the extract was formulated as a topical cream and evaluated physical properties and stability. The results showed good aspects for its potential to be formulated and used in therapy, but its therapeutic efficacy should be studied and evaluated in animals and then clinically. Furthermore, since it is a world spread plant special in tropical regions such as Iran, providing and supplying the extract has economical profits.

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