INTRODUCTION

It is widely known that the largest organ in the body is the skin; it is about 20 ft² of total area. It is main purpose for body protection from invasive elements and microorganisms. It also helps regulating the temperature of the body and allows the sense of touch, cold, and heat [1]. There are different factors that affects on the skin such as ultraviolet (UV) radiation, for example, sun damage, dehydration, and microorganisms like bacteria invasion, mechanical trauma, and physical injuries [2]. The chemical products used for cosmetics or skin care are gaining attention because of the negative effect on skin and health. Furthermore, the chemical additives of skin care products may lead to skin irritation and allergic reactions [3]. Such as the harmful effect of steroids chemical agents when used for skin bleaching. Recently, the herbal or medicinal plants were used as a source for skin care products. The extracts of herbs showed more powerful antioxidant activity and keep the skin looking not only healthy but also years' younger [4]. The most benefit of herbal extracts in skin care belongs to their natural agents such as omega3, vitamins, and minerals. Furthermore, the plant part extracts contain natural nutrients like Vitamin E that keeps skin healthy [5]. The safflower (Carthamus tinctorius L.) plant (Fig. 1) is considered as one of the most important medicinal plants, the seeds of this plant are rich in edible oil, and the components of its oil are unsaturated fatty acids such as oleic acid (omega 9), linolic acid, linolenic acid (omega 6), and palmitic acid [6]. All these unsaturated fatty acids have different benefits for skin diseases or care. The aim of this study was to formulate and evaluate safflower oil as nutritive skin cream and study its clinical effect.

MATERIALS AND METHODS

Materials

Plant material seeds of safflower plants were collected from safflower farm or field at Karbala town during seeding stage (May 2017).

Methods

Safflower oil extraction

Safflower oil was extracted from seeds using expeller pressing (cold pressing). The extraction process was done in AL-Raed factory for vegetable oils production. After extraction, the oil was kept at low temperature because safflower oil is primarily composed of less stable polyunsaturated and monounsaturated fatty acids. It can be particularly susceptible to degrade by heat, air, and light which trigger and accelerate oxidation [7].

Physical examination of oil

Density, refractive index (using digital refractometer, Abbe type universal, Germany), and specific gravity for safflower oil are determined.

Methods:

After collecting the safflower seeds, the oil was extracted using an expeller or cold pressing. Physical parameters of oil were determined. Determination of unsaturated fatty acids was done by gas-liquid chromatography (GLC). The oil is then placed in an emulsifier to form cream using various additives and all formulas evaluated according to physical properties, PH, and viscosity.

All symptoms such as skin damage by sunlight, skin aging, oxidative damage after sunburn or after chemical treatments, all of these conditions have recovered. Statistical data analysis was carried out using Statistical Analysis System, and all recorded data for analysis of variance and least significant difference were at least the significant difference at level 0.01.

Results:

The results of the GLC analysis indicated that safflower oil contains five different fatty acids, including linoleic acid (56.37%), linolenic acid (15.02%), stearic acid (2.37%), oleic acid (14.83%), and palmitic acid (7.91%). Refractive index values, density, and specific gravity were 1.476, 0.921 g/cm³, and 0.925, respectively.

The results of a clinical study showed the effect of safflower cream as an antioxidant which protected the skin in particular from oxidative damage after sunburn and reduced the symptoms of skin aging. This effect was evident in both concentrations 10% and 15% when compared with control.

Control response rate, 10% of safflower cream, and 15% of safflower cream were reached to 76%, 85%, and 92% within 2 weeks of treatment, respectively.

Conclusion:

The study showed the importance of safflower oil as a source of omega-3 and contains various unsaturated fatty acids which act as an antioxidant to restore skin health and aging resistance. This study approved that safflower oil characteristics can make it the main ingredients in the preparation of topical agents for the treatment of various skin problems.

Keywords: Safflower, Clinical application, Nutritive.
Gas-liquid chromatography (GLC) analysis of oil
Gas chromatography technique was used to determine fatty acids among the completion of its methyl esters preparation. This technique was conducted in the laboratory of sciences and technology. Adding 3 ml of n-heptane in a test tube was performed to accomplish esterification. Glycerol supernatant was obtained by vortexing the tubes for 5 min, and 0.2 ml from samples was used to conduct analysis [8].

Model GC 1000 of GLC, according to Dany co., Italy, with flame ionization detector and DS 1000 interface integrator which was attached to the column for the purpose of methyl ester separation was 0.33 mm diameter from the inner side and 30 mm of length. The temperature of the columns was fixed to be from 100 to 200°C with a gradual increment of 30°C per min. Then, it was stopped and again raised at a rate of 10°C/min until reached the final temperature. The detector and injector's temperature was fixed at 200°C until reached the final temperature.

**Cream: Preparation of safflower**
Oil in water (O/W) emulsion-based cream (semisolid formulation) was formulated. The emulsifier (stearic acid) and other oil soluble components (safflower oil and cetyl alcohol) were dissolved in the oil phase (almond oil) and heated to 75°C. The preservatives (methyl paraben and propylparaben) and other water-soluble components (triethanolamine and propylene glycol) were dissolved in the aqueous phase and heated to 75°C. After heating, the aqueous phase was added in portions to the oil phase with continuous stirring until cream is formed then left at room temperature until cooled [9].

**Characterization of safflower cream formulas**

**Physical properties**
The cream was observed for color, odor, and appearance [10].

**Determination of pH**
About 0.5 g of the cream weighed and dissolved in 50 ml distilled water, and its pH was measured [11].

**Viscosity**
Rheological measurements regarded as sensitive tools for detecting structural changes in pharmaceutical creams and should be regarded as an integral part of the quality evaluation of pharmaceutical creams. The viscosities of formulated safflower creams were measured by Brookfield viscometer (DV-II) at room temperature [12].

**Clinical study**
The clinical study was carried out at Al-Razi center of alternative medicine, Baghdad, Iraq. Ninety patients were included in this study and divided into three groups randomly, group treated with conventional treatment (nutritive cream vitamins A, C, and E lipolic complex) as control, Group B treated with 10% safflower cream, and Group C treated with 15% safflower cream. All symptoms such as skin aging, skin damaged by the sunlight, and oxidative damage after sunburn or after chemicals treatments were followed for 6 months. All clinical studies were conducted in accordance with the Ethical Committee of College of pharmacy/Al-Mustansiriya University.

**Statistical analysis**
The analysis of the statistical data was conducted by the Statistical Analysis System statistical program, and all the recorded data were applied for the analysis of variance and least significant difference at level 0.01 was used to compare the studied parameters [13].

**RESULTS**

**GLC analysis of safflower oil**
The results were referred that safflower oil had different five fatty acids including linolic acid (Lin) (56.37%), linolenic acid (L) (15.02%), stearic acid (S) (2.37%), oleic acid (O) (14.83%), and palmitic acid (P) (7.91%) as shown in Figs. 1-3.
Table 1: Components of safflower cream formulas

| Ingredients          | Formula (% w/w) |
|----------------------|------------------|
|                      | F1               | F2               |
| Safflower oil        | 10               | 15               |
| Stearic acid         | 6                | 6                |
| Glycer alcohol       | 3                | 3                |
| Almond oil           | 5                | 5                |
| Propylene glycol     | 4                | 4                |
| Triethanolamine      | 2                | 2                |
| Methylparaben        | 0.05             | 0.05             |
| Propylparaben        | 0.05             | 0.05             |
| Distilled water      | QS               | QS               |

Table 2: Age and sex distribution in the study population

| Distribution | Control | 10% safflower cream | 15% safflower cream | Total n (%) |
|--------------|---------|---------------------|---------------------|-------------|
| Age (years)  |         |                     |                     |             |
| 19–24        | 20 (66.66) | 18 (60)            | 23 (76.66)          | 61 (67.7)   |
| 24–30        | 3 (10)   | 8 (26.66)           | 3 (10)              | 14 (15.55)  |
| 30–40        | 4 (13.33)| 2 (6.66)            | 2 (6.66)            | 8 (8.88)    |
| 40–55        | 3 (10)   | 2 (6.66)            | 2 (6.66)            | 7 (7.77)    |
| Sex          |         |                     |                     |             |
| Male         | 4 (13.33)| 8 (26.66)           | 9 (30)              | 21 (23.33)  |
| Female       | 26 (86.66)| 22 (73.33)        | 21 (70)             | 69 (76.66)  |
| Total        | 30 (100) | 30 (100)            | 30 (100)            | 90 (100)    |

Table 3: Patient’s response for safflower cream in different time intervals

| Groups          | 3 weeks on treatment | 4 weeks on treatment | 2 weeks after end of the treatment |
|-----------------|----------------------|----------------------|-----------------------------------|
| Control         | 71%                  | 75%                  | 73%                               |
| 10% safflower cream | 76%            | 81%                  | 80%                               |
| 15% safflower cream | 85%                | 92%                  | 91%                               |

The study showed the importance of safflower oil as a source of omega-3 and contains various unsaturated fatty acids which act as an antioxidant to restore skin health and aging resistance. According to the results of this study, safflower oil characteristics make it the main ingredients in the preparation of various natural topical agents for the treatment of various skin problems.

**AUTHOR’S CONTRIBUTIONS**
All the work was carried out by Ibtihal Abdulkhaidh Dakhil, Ibrahim S. Abbas, and Nidhal K. Maraie.

**CONFLICTS OF INTEREST**
The authors declared that they have no conflicts of interest.

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**CONCLUSION**
Fatty acids were suggested that essential fatty acids may diminish the rate of inflammation with acne and also reduce photodermatitis-induced sun sensitivity. Other studies found that psoriasis treatment also includes medication and essential fatty acids.