

Original Article

DEVELOPMENT AND *IN VITRO* EVALUATION OF A NEW TOPICAL O/W EMULGEL FROM FRUIT EXTRACT OF *PYRUS COMMUNIS*

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ABSTRACT

Objective: The aim of the present study was to develop a new topical dosage form containing *Pyrus communis* fruit extract. Developed formulation was O/W Emulgel which was evaluated by its *in vitro* tests and its stability studies at different storage conditions.

Methods: Hydroalcoholic *Pyrus communis* extract was prepared by the maceration process. A 4% *Pyrus communis* emulgel was prepared by the combination of emulsion and gel at a specific temperature and mixing through homogenizers. The formulations having different concentration of carbopol 940 (gelling agent) were placed at 8 °C, 25 °C, 40 °C and 40 °C+75%RH for 3 mo in order to find out the most stable formulation. After the selection of final emulgel formulation was eventually further evaluated for *in vitro* studies such as phase separation, centrifugation, rheology, pH, conductivity, organoleptic properties and mean droplet size over a period of 12 w at 8 °C, 25 °C, 40 °C and 40 °C+75%RH.

Results: *In vitro* evaluation of the selected *Pyrus communis* emulgel formulation showed good resistance to phase separation on centrifugation, conductivity gradually increases due to oil in water emulgel and pH of formulation was gradually decreased. The rheological behavior was non-Newtonian pseudoplastic and showed shear thinning fluid behavior. Mean droplet size of *Pyrus communis* emulgel was 16.0±0.20 µm and after 90 d droplet size was 16.7±0.55 µm at high storage temperatures at 40 °C and 40 °C+75RH and no significant changes were observed at normal storage conditions at 8 °C and 25 °C.

Conclusion: *Pyrus communis* emulgel fresh fruit extract showed stable formulation at different storage conditions. This new formulation will be a good addition to pharmaceutical dosage forms made from traditionally used plants.

Keywords: *Pyrus communis*, Emulgel, Stability testing, *In vitro* evaluation

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INTRODUCTION

Fruits are an important part of our diet. It provides nutrition and energy to our body. Traditionally, different fruit extracts have been used in medicines for internal and external diseases as a remedy. Some fruits like pear are commonly used in Pakistan having many health benefits [1]. Diet-conscious peoples are taking it as it helps in the reduction of weight. This fruit has very less caloric content. It is rich of healthful components like carbohydrates, minerals, vitamins, protein, fat, fibers, etc. The peel and pulp show better phenolic constituents and Flavonoid as compared to seed of a pear [2]. *Pyrus Communis* has a better composition of Flavonoid contents, anthocyanin, tannins, and polyphenol. *Pyrus Communis* is a rich source of vitamin C, folic acid, dietary fiber, Potassium, Tyrosine, Aspartic acid. Natural bioactive agents are responsible for color, odor, appearance and taste of fruit [3-5].

Pyrus Communis was used in folk medicines as diuretics as it is rich in fiber and low in sodium. In diarrhea its astringent and antiseptic properties help in the treatment of colitis. It helps in cholesterol reduction so helps in controlling obesity, cardiovascular diseases and cancer. Also reported for laxatives, hypertension properties. It is very suitable diet for diabetics due to its low-calorie content. It has a high amount of potassium which, along with calcium, helps in bone formation and nervous systems. So help in the growth of children. After growth helpful in the maintenance of bones and nervous system. Due to rich sources of vitamin C it has strong antioxidant potential [6, 7].

Fruit Extract has been used topically by ladies in Pakistan as a scrubber. Fruit extract help in glowing of skin as acting as anti-aging and reduces wrinkles. It is a very good antiseptic and analgesic [7]. But unfortunately, no single pharmaceutical topical dosage form has been available yet having pear extract. Although many topical dosage forms having plant extracts had been formulated by different researchers like cream, ointment, gels and emulgel [8]. It is noted that emulgel is the best formulation as it is having both benefits of

gel and emulsion. It has the best drug loading capacity and provides fast drug release from the formulation. Although it provides better penetration of drug to skin [9-11].

The present study aims to formulate water in oil emulgel having *Pyrus communis* plant extract. Formulation is tested for its stability under different temperature conditions. O/W Emulgel qualifies the stability tests afterward the stable formulation is tested for other *in vitro* tests. The prepared formulation is the new topical dosage form having *Pyrus communis* extract and will be a promising addition in the health care system.

MATERIALS AND METHODS

Chemicals

The chemicals were purchased by Merck K GaA Darmstadt, Germany (Liquid paraffin, span 20, tween 20, propylene glycol, methyl parabin, analytical grade methanol, triethanolamine and carbopol 940). Water was distilled fresh from the laboratory.

Apparatus

Rotary evaporator (EYELA-CA-III, Rika-KiKai, Tokyo, Japan), pH meter (WTW pH-197i, Germany), Conductivity meter (WTW COND-197i, Germany), Centrifugation machine (EBA 20. Hettich, Germany), Rheometer (DV-III Ultra, Brookfield engineering laboratory, USA), Optical microscope (Eclipse E200, Nikon, Japan).

Fruit material

The fresh whole fruit of *Pyrus communis* was used as the active drug agent for medicinal purposes. These were collected from Azad Kashmir. Then these fruits were identified from Quaid-I-Azam University in the department of plant sciences by Dr. Muhammad Zafar Ph. D. (QAU) Herbarium Botanist and voucher specimen's number certificate was 805.

Preparation of *Pyrus communis* extract

1 kg fresh whole fruit except seed of *Pyrus communis* was cut into slices and then ground with 300 ml of distilled water. A paste made and added 800 ml analytical grade methanol to make final volume 1000 ml. 80% methanol and water (v/v) ratio mixture, covered with aluminum foil wrapping for 3 d at a 25 °C room temperature in a 5 liter beaker. The hydroalcoholic fruit extract was shaken after 24 h daily in order to improve the solubility of fruit constituents with solvents. The extract was obtained from the macerated mixture by filtration using muslin cloth. Then this filtrate was again passed through whattman no.1 filter paper for further filtration. The filtered extracts were concentrated and evaporated by using a rotary evaporator at a speed of 40 rpm at the temperature of 40 °C and refrigerator (chiller) 5 °C. The dried concentrated extract was stored in a refrigerator at 8 °C until used for further characterization study.

Preparation of emulgel

For emulsion preparation first of all measure the ingredients and then separately heat, oily phase and aqueous phase at 75 °C and then mixes both phases and mixed them under a speed of <70rpm in a homogenizer. Next Step was the preparation of gel. In-gel preparation measure the ingredient carefully and mixed 1.5 % of cabopol940 in distilled water in a homogenizer at a gentle speed to make final weight 100 gm. When the gel was formed so add triethanolamine solution (pH adjusting agent) few drops to stable the gel at pH lie between 6.0-5.5 by using pH meter. Mix the emulsion, gel and 5% *Pyrus communis* extract in a homogenizer at the speed of 2000 rpm for 10 min and then reduced to 1000 rpm for 5 min and again homogenized for 5 min at the speed of 500rpm. Final emulgel was prepared and cover the beaker with aluminum foil and placed at different temperatures 8 °C, 25 °C, 40 °C and 40 °C+75% RH.

Stability studies

Stability studies were performed in two stages i.e. one was done in two months and this period was called preliminary studies. The second was done in a two month period divided into different storage temperature, i.e. 8 °C, 25 °C, 40 °C, 50 °C and 40 °C+75RH. Most stable finally selected emulgel was obtained from these studies and freshly prepared selected emulgel again kept for two months at different temperatures, i.e. 8 °C, 25 °C, 40 °C, 50 °C and 40 °C +75%RH [12-14]. Base formulation (without *Pyrus communis* extract) is also tested for its stability under all these conditions.

Data analysis

All the results are presented as a mean±standard deviation (SD). Image analyzing software (Digimizer) was used to perform particle size analysis. One way analysis of variance (ANOVA) was used to analyze the data for rheology. The level of significance adopted was p<0.05.

In vitro characterization of *Pyrus communis* extract based emulgel

pH

This test was performed by dipping lobe of pH meter in the formulation. Formulation and base pH was observed at 8 °C, 25 °C, 40 °C, 40 °C+75% RH temperature conditions. Beakers of formulation and base were covered with aluminum foil and placed at different temperature for three month study periods.

Conductivity

Conductivity test was carried out by placing lobe of conductivity meter into the beakers which were filled by formulation at different storage conditions. A probe of Electrical conductivity meter was dipped into the formulation until a stable reading was measured and the average value was noted down.

Centrifugation

Centrifugation test was carried out by placing 2g of formulation and base, stored at different conditions, in the 15 ml centrifuge tube and centrifuged for two runs of 10 min, at 5000 rpm. At the end of each cycle, tubes were investigated macroscopically for the presence of any possible phase separation.

Rheology

Rheological properties of the formulation were investigated using a cone and plate type rheometer equipped with a circulating system for temperature control. Rheological measurements were made at 25±1 °C using a CP41 spindle. Shear rate was progressively increased from 20-86/s to construct the rheograms and data obtained was mathematically analyzed by a Brookfield programme, Rheocalc version V 1.01 according to the power law analysis as mention in equation 2

$$T=K D n \dots\dots\dots (2)$$

Where T is shear stress, D is the shear rate; K is consistency index and n is the flow index [14].

Microscopic evaluation

The emulgel morphology and particle size were described by an optical microscope coupled to a high-resolution digital camera. Micrographs were collected by using Mnisee version 1.1 Image analyzing software, at 100 x magnification. A small quantity of w/o emulsion was smeared on the glass slide and diluted it with external phase. Samples were covered slip with care to avoid sample damage by shear stress. The mean droplet size was reported by using calibrated ocular micrometer. The data were obtained from 20 various micrographs of the sample.

RESULTS

pH

The pH was observed to the *Pyrus communis* emulgel for the 12th week study period. The pH of freshly prepared *Pyrus communis* emulgel was 5.87 which were decreased to 5.00 after the 12th week of the study period as shown in table 1. Base pH was higher than formulation pH.

Conductivity

The freshly prepared *Pyrus communis* emulgel had conductivity was 90.79µ S/cm which increased with the passage of time to 225 µ S/cm after 12th weeks as shown in table 1. Higher increased was observed at 40 °C and 40 °C+75%RH. The less increased was observed at 8 °C and 25 °C. Formulation showed less conductivity than the base.

Centrifugation

Pyrus communis formulation and the base was kept at 8 °C, 25 °C, 40 °C and 40 °C+75%RH storage conditions and it is observed that formulation placed at 8 °C and 25 °C did not show any phase separation at the complete period of study. Formulation at high temperature 40 °C and 40 °C+75%RH was shown little effect on it as slight phase separation was observed after the 12th week of the study period. The *Pyrus communis* emulgel showed better long term stability as no phase separation was observed. Similarly, base also did not show any phase separation.

Rheology

The relationship between shear rate and viscosity for formulations at various conditions after different time interval was shown that flow curves were non-linear which showed the non-Newtonian, the pseudo plastic behavior of formulation during the study period. Such characteristic was desirable in the typically applied formulations which were used in pharmaceutical and cosmetic products. The values of rheological parameters are shown in table 2. The consistency index (CI), flow index (FI) and confidence of fit were shown in the table. Power law analysis method was used in this study.

Microscopic evaluation

The photomicrographs of freshly prepared *Pyrus communis* emulgel and after the 12th week in various storage conditions were shown in fig. 1. The freshly prepared *Pyrus communis* emulgel droplets were spherical in shape. The shape of the particles was not changed in the 12th week of the study period. The mean droplet size of emulsion was found to be within macroemulsion range (1-100 µm) for 12th week of study periods which kept at different temperature and humidity conditions.

Table 1: pH and Conductivity at 8 °C, 25 °C, 40 °C and 40 °C+75%RH of *Pyrus communis* emulgel, after 30 d, after 60 d and after 90 d

Reading schedule	pH							
	8 °C		25 °C		40 °C		40 °C+75%RH	
	B	F	B	F	B	F	B	F
Fresh Reading	6.8±0.03	6.4±0.03	6.8±0.03	6.4±0.05	6.8±0.03	6.4±0.03	6.8±0.02	6.4±0.03
After 24 H	6.8±0.04	6.4±0.05	6.8±0.03	6.4±0.03	6.7±0.02	6.3±0.03	6.7±0.01	6.3±0.04
After 72 H	6.7±0.03	6.3±0.04	6.7±0.03	6.3±0.03	6.6±0.05	6.1±0.03	6.5±0.02	6.0±0.03
After 7 D	6.6±0.02	6.1±0.03	6.5±0.04	6.0±0.04	6.4±0.01	5.9±0.05	6.3±0.02	5.7±0.02
After 14 D	6.5±0.03	6.0±0.05	6.4±0.05	6.0±0.02	6.3±0.02	5.8±0.04	6.2±0.04	5.6±0.03
After 28 D	6.4±0.03	5.8±0.04	6.3±0.04	5.7±0.03	6.2±0.02	5.5±0.03	6.1±0.05	5.3±0.05
After 45 D	6.3±0.03	5.7±0.03	6.2±0.01	5.6±0.04	6.1±0.03	5.4±0.01	6.0±0.01	5.2±0.04
After 60 D	6.2±0.02	5.6±0.04	6.1±0.02	5.5±0.01	6.0±0.04	5.4±0.02	5.9±0.03	5.3±0.03
After 75 D	6.1±0.03	5.4±0.05	6.0±0.05	5.3±0.02	5.9±0.03	5.1±0.03	5.8±0.04	5.0±0.04
After 90 D	6.0±0.03	5.3±0.05	5.9±0.03	5.2±0.01	5.8±0.04	5.0±0.04	5.7±0.03	5.0±0.05
Conductivity								
Fresh Reading	173±0.03	91±0.09	173±0.1	91±0.2	173±0.01	91±0.1	173±0.05	91±0.06
After 24 H	174±0.02	92±0.06	175±0.06	92±0.1	178±0.02	94±0.21	179±0.05	95±0.05
After 72 H	179±0.02	95±0.05	180±0.07	96±0.11	181±0.03	99±0.18	184±0.04	101±0.05
After 7 D	183±0.02	102±0.06	184±0.1	105±0.23	191±0.02	110±0.09	199±0.06	120±0.04
After 14 D	186±0.01	125±0.07	188±0.06	133±0.09	193±0.02	145±0.08	201±0.03	156±0.04
After 28 D	193±0.04	155±0.08	189±0.08	159±0.1	199±0.03	167±0.08	206±0.03	168±0.05
After 45 D	199±0.01	159±0.09	196±0.2	161±0.21	201±0.05	169±0.06	210±0.04	170±0.05
After 60 D	201±0.05	169±0.09	200±0.05	164±0.06	215±0.04	178±0.06	220±0.05	177±0.03
After 75 D	207±0.01	173±0.06	209±0.06	177±0.08	218±0.04	191±0.05	234±0.04	188±0.08
After 90 D	212±0.09	186±0.08	214±0.08	189±0.07	229±0.03	197±0.06	234±0.06	202±0.07

mean±SD (n=3)

Table 2: Consistency index, flow index and confidence of fit at 8 °C, 25 °C, 40 °C and 40 °C+75%RH of *Pyrus communis* emulgel, after 30 d, after 60 d and after 90 d

After	Temperature	Fresh	8 °C	25 °C	40 °C	40 °C+75% RH
30 D	Consistency Index	2350	2200	2160	2010	1970
	Flow Index	0.15	0.16	0.17	0.19	0.21
	Confidence of Fit	93.2%	94.7%	95.8%	96.6%	97.3%
60 D	Consistency Index	2350	2264	2175	1940	1634
	Flow Index	0.15	0.16	0.17	0.20	0.23
	Confidence of Fit	93.2%	95.2%	96.3%	97.0%	98.8%
90 D	Consistency Index	2350	2108	2056	1890	1542
	Flow Index	0.15	0.17	0.18	0.22	0.25
	Confidence of Fit	93.2%	95.9%	96.8%	97.1%	98.4%

Table 3: Photomicrographs of freshly prepared *Pyrus communis* emulgel and after 12th week in various storage conditions

Time period	8 °C	25 °C	40 °C	40 °C+75%RH
After 30 d	16.0±0.30	16.0±0.60	16.4±0.50	16.1±0.50
After 60 d	16.2±0.63	16.4±0.72	16.5±0.50	16.7±0.60
After 90 d	16.6±0.60	16.7±0.55	16.8±0.30	16.9±0.20

mean±SD, RH= 75% Relative humidity, (for number of droplets n = 20)



(A) Freshly prepared *Pyrus communis* emulgel



(B) After 12 w of storage at 40 °C+75%RH

Fig. 1: Mean droplet diameter at various time intervals

DISCUSSION

Fruits are the source of energy. Not only they provide nutritional support to us, but also used as medicine. Orally and topically a lot of fruits are used in the external and internal dosage forms. In the present study, a new emulgel was prepared. A lot of researchers worked with fruit extracts for developing topical formulations [15]. *Pyrus communis* is one of the gifts of God. Fruit is full of healthy constituents like vitamin C, carbohydrates, and minerals. Peoples use it orally for weight conscious peoples. Also used for diarrhea, hypertension and cardiac patients. Ladies used it for treatment of acne, lip balms and scrubbers. It is also good for hair. Until now no single pharmaceutical topical dosage form is present containing *Pyrus communis* extract. Normally formulations containing plant extracts have a stability issue. So in this study a new topical emulgel containing *Pyrus communis* extract is prepared. Emulgel formulation containing *Pyrus communis* extract and base (without *Pyrus communis* extract) is tested for its stability by keeping the formulation at 8 °C, 25 °C, 40 °C, 40 °C+75%RH conditions. Formulation successfully qualified all conditions. The best storage temperature suggested is 25 °C±5 °C as at 40 °C after 12 w formulation showed a little degradation. The formulation has been tested for other *in vitro* tests like pH, conductivity, centrifugation and rheology at these temperature conditions. For topical dosage forms pH should be in the range of 5.5. to 6.5 and the present formulation fit best in this range after 12 w testing. The pH of the formulation was decreased with the passage of time due to the acidic nature of fruit extract. This supports the common use of this fruit as ladies in Pakistan use its fruit extract as household remedy for acne. Moreover, conductivity test was gradually increased in results of conductivity due to the movement of ions, but the formulation showed less conductivity as compared to the base formulation. The centrifugation test is an efficient stability test which physically used to measure the phase separation and liquefaction ability of formulation. The principle of this test was checked the effect of centrifugal force on the formulation by separating two different phases, i.e. these phases may be two immiscible liquids or one liquid and one insoluble solid. Phase separation of the formulation serves as a test to determine the stability of emulgel [16]. In our study the formulation described the slightly liquefaction after 75 d study periods due to high storage temperature (40 °C and 40 °C+75%RH). At higher temperatures, slight phase separation was occurring due to lowering of viscosity of oil phase under centrifugal force [16]. Both base and formulation showed similar behavior. This study showed that non-Newtonian, the pseudoplastic behavior of the formulation was not changed even under thermal stress over a period of time, describing the physical stability [17]. Rheology is concerned with the production and application of emulgel. Rheological parameters are very unique in determining the physical stability of the emulgel during the study period [18]. On the other hand, rheological results showed that a decreased occurred in the consistency Index of the formulation at various temperatures during storage conditions [19, 20]. Droplet

size is one of the most vital physical stability characteristics of the formulation which was used for topical formulation for cosmetic or dermal purposes. The small size of droplet was shown the less chance of formulation towards coalescence and sedimentation phenomena against gravitational forces [20]. In this study droplet size analysis showed that the emulgel had a small droplet size within the macro emulgel size range. The emulgel having *Pyrus communis* extract showed little increased in the droplet size of formulation at 8 °C and 25 °C of storage conditions. Meanwhile, an increase in droplet diameter was observed at higher temperatures, i.e. 40 °C and 40 °C±75%RH. It is stated that at higher temperature, the change in viscosity of continuous phase that viscosity decreased, which allow more frequent collision between the droplets and result in the increase of droplet size.

CONCLUSION

In this study the prepared w/o emulgel having *Pyrus communis* extract successfully qualify *in vitro* tests. The developed *Pyrus Communis* extract w/o emulgel containing good stability with proper resistance to phase separation, pH, conductivity, pseudoplastic behavior and mean globule diameter in a narrow range over a specified period of time. New topical emulgel containing *Pyrus Communis* extract will be a good addition to pharmaceutical topical dosage forms. It is very necessary for the young researchers to work on the evidence base medicine and formulate new stable formulations. Such formulation developments will open new avenues in the healthcare system.

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AUTHORS CONTRIBUTIONS

Both Authors contributed equally in the designing, conducting and preparation of the manuscript of this research work.

CONFLICT OF INTERESTS

No conflicts of interest associated with this work

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