ARTICLE

Preformulation studies of an emulsion containing commercially available argan oil

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ABSTRACT

Background: Argan oil has gained popularity in recent years due to its potential anti-inflammatory and antioxidant properties. The present pre-formulation study sought to investigate the suitability of using commercially available argan oil as a unique pharmaceutical emulsion formulation for oral consumption. This research aimed to develop an efficient pre-formulation strategy for oil-in-water emulsion containing argan oil and optimize the formulation's optimum stability as a pharmaceutical dosage form.

Methods: Various analytical and physical characterization techniques were employed in making an emulsion, such as organoleptic analysis, pH level, viscosity, particle size distribution, gravimetric test, and dye method test. The three formulations (A, B, and C) gave different results for the sizes of oil droplets, appearance, taste, and compatibilities.

Results: Among the tested formulations, formulation A, containing 5 ml argan oil, exhibited a cloudy white appearance, hazelnut-like taste and texture, higher oil retention, and improved droplet size dispersion (0.58 µm - 116.21 µm). The results indicated that all three formulations have acidic pH values 4.82-5.84.

Conclusion: Formulation A demonstrated notable attributes, making it the optimal choice for the oil-in-water emulsion containing argan oil. Addressing compatibility concerns and assessing sensory attributes, pH levels, and particle size distribution successfully achieved the desired pharmaceutical elegance, laying a promising foundation for developing stable and effective oral emulsions.

INTRODUCTION

Argan oil, extracted from the Argania spinosa tree indigenous to Morocco, is uniquely positioned in the botanical world celebrated for its diverse applications and potential health benefits. Recognized for its bio-ecological importance, this oil is a prized resource in North Africa (Mansour et al. 2018). Two main types of argan oil exist: cosmetic and culinary. The cosmetic variant, obtained through a cold-pressing method using unroasted fruit kernels, has long been favored for skincare and haircare (Taribak et al. 2013). In contrast, culinary argan oil,

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produced from roasted kernels, offers a flavor akin to hazelnuts, enhancing culinary experiences (Gharby & Charrouf 2022).

Argan oil primarily comprises triglycerols and essential fatty acids (Table 1). Vital fatty acids include oleic acid (43-50%), linoleic acid (29.3-37%), stearic acid (4.3-7.2%), and palmitic acid (10-15%) (Gharby & Charrouf 2022). These fatty acids contribute to the oil's potent antioxidant and anti-inflammatory effects, potentially mitigating chronic diseases like heart disease and cancer. The high concentration of oleic acid (C18:1), constituting 40-50% of the total fatty acids, is a notable component known for its monounsaturated omega-9 fatty acid properties, linked to a reduced risk of cardiovascular disease (Gharby & Charrouf 2022). Likewise, linoleic acid (C18:2), another essential fatty acid present in argan oil, contributes to the oil's antioxidant effects and potential to prevent chronic diseases (Gharby & Charrouf, 2022).

Table 1: Chemical composition of argan oil

Compositions	Percentage
Physicochemical	
Density at 20°C	0.908-0.918
Specific absorbance measured at 270nm.	Max 0.4
Acid Value in mg KOH/g	Max 4.0
Peroxide Value in Meq.	Max 10.0
$O2$ /Kg	
Sterol	Max 0.2
Cholesterol	Max 1.5
Campesterol	Max 1.0
Stigmasterol	34-44
Spinasterol	44-50
Schottenol	4-7
Delta 7 Avenasterol	
Fatty acid	10-15
Palmitic acid (C16:0)	4.3-7.2
Stearic acid (C18:0)	43-50
Oleic acid (C18:1)	29.3-37
Linoleic acid (C18:2)	

However, despite its vast array of benefits, concerns regarding the potential adverse effects of argan oil have been raised. Allergic contact dermatitis, mainly observed in sensitive individuals, has been documented as a skin reaction upon topical application (Foti et al. 2014). A rare but severe potential side effect includes anaphylaxis, notably when ingested raw (Veraldi 2016).

In pharmaceutical realms, the utilization of argan oil has expanded to oil-in-water emulsions, offering a promising drug delivery system. Understanding the factors influencing the pharmaceutical elegance of such emulsions is crucial. Various components, the droplet size, oil-to-water ratio, and emulsifier choice significantly affect the emulsion's stability and quality. The pH range is a critical factor; maintaining an appropriate pH range minimizes phase separation and maximizes stability (Camacho et al., 2015).

This research endeavors to bridge a significant gap by delving into argan oil's potential for dosage form development and pinpointing the optimal oil content in oral emulsions — a domain with limited studies. The objectives are twofold: the general aim was to devise an efficient preformulation strategy for creating an oil-in-water emulsion containing argan oil, while the specific purpose was to conduct and optimize the formulation to achieve maximum pharmaceutical elegance as a stable dosage form.

MATERIALS AND METHODS

Materials and Reagents

This study utilized Argan oil (*Etsy.com, ArganOilDirect),* Tween 80 (*Aishite Trading),* chocolate flavorant (*Aishite Trading),* and sucrose *(2:1 ratio of sugar and water).* The Adamson University - Pharmacy Laboratory provided the laboratory apparatus, Overhead stirrer *(Onilab OS40-Pro),* pH meter *(Horiba® D-51 series), and* Viscometer *(Brookfield D1 series),* and supplies used in the experiment.

Compatibility testing

Compatibility testing was conducted to assess the interactions between the excipients and the argan oil. Differential scanning calorimetry (DSC) was used to test the compatibility of the excipients before formulation. A 1:1 combination of the argan oil and excipients was prepared and sent to ADMATEL in Taguig City for testing.

Preformulation of Emulsion

Different formulations of an oil-in-water emulsion were prepared (Table 2). Moreover, the different concentrations of argan oil are tested to determine the pharmaceutical elegance between formulations. The deionized water was placed in a 250 ml beaker at a 100 rpm speed; after adding the tween 80, raise the speed to 250 rpm. Once the sucrose was partially dissolved, the speed of the stirrer was increased to 350 rpm. The argan oil was added to the continuous phase drop by drop at 400 to 440 rpm. A minimum of 15 minutes was spent homogenizing the mixture with an overhead stirrer spinning at 450 rpm to complete the procedure. (Mezger 2011)

Table 2: Formulation of an oil-in-water emulsion in different oil concentrations.

Ingredients	Use	Formulation A	Formulation B	Formulation C
Argan oil	API[1]	5 ml	10 ml	15 ml
Tween 80	Emulsifier	4.2 ml	4.2 ml	4.2 ml
Sucrose	Sweetener	15.8 ml	20.8 ml	20.8 ml
Deionized Water	Solvent	35 ml	25 ml	20 ml

[1]API; Active Pharmaceutical Ingredient

Quality Control Tests for Preformulated Oil-in-water Emulsion

Organoleptic Test

The different formulations were evaluated for their appearance, taste, odor, and texture to determine their pharmaceutical elegance. Pure argan oil has a light-dullish yellow color and a hazelnut-like taste and aroma (Gharby & Charrouf 2016).

pH

The pH of the preformulated oil-in-water emulsion was measured using a pH meter. The expected results range from 3.5 to 7 (Juttulapa et al. 2013)

Viscosity

The viscosity of the emulsion was determined using a viscometer for 15 minutes at 60 rpm, using spindle #2 at 23 °C. The recommended viscosity for the emulsion is within low viscosity (10-100 cP) to moderate viscosity (100-1000 cP). These viscosity values allow easy administration, swallowing, and spreading within the oral cavity while ensuring sufficient emulsion droplets' stability and control (Shimizu et al. 2013).

Particle Size Distribution

The testing was conducted in NASAT Labs – Water and Environmental Testing Laboratory in Cabuyao City, Laguna. The emulsion samples were subjected to laser diffraction analysis. Furthermore, the higher the number of smaller dispersed particles, the more stable the formulation (Nam et al. 2021).

Oil-in-water emulsion test

a. Gravimetric Test

The procedure started by weighing a clean filter paper. It was then placed in a funnel with a bit of hexane. The stirred formulations were transferred through the paper. The filtered excipients were collected in a beaker. The filter paper was dried at 105°C for 30 minutes, then weighed. Confirmation of the oil-in-water emulsion was performed by gravimetric analysis, ensuring that the water percentage exceeds the oil percentage and observing oil retention on the filter paper (Humaish et al., 2020).

b. Dye Method

The orange dye was used for the dye method test. This method was performed on triplicate replications for each formulation. It was observed through a microscope. The droplets from the sample were examined according to size and if the emulsion was homogeneously distributed (Pramudono et al. 2021). If the continuous phase is yellow-orange to yellow, the emulsion is of the o/w type, as water is in the external phase, and the colorant will dissolve.

RESULTS AND DISCUSSION

Compatibility Testing

Results indicated excipient compatibility with argan oil, except for chocolate flavorant. The latter displayed a notable heat flow curve shift at around 149.27 °C, signaling incompatibility. Consequently, chocolate flavorant was omitted due to significant melting point discrepancy, raising concerns about formulation stability (Gharanjig et al. 2020).

Organoleptic

All three formulations were compared to the typical appearance of oil-in-water-like milk (Figure 1). They met the standards for an oil-in-water emulsion concerning color, taste, odor, and texture (Table 3). Emulsions with various structural designs, such as gel, cream, and oily textures, often appeal to consumers, showcasing their versatility in product development (Chung and McClements 2015). Formulation A stood out for its superior appearance and taste, attributed to a well-dispersed Argan oil concentration.

A – Formulation A; B – Formulation B; C – Formulation C

Figure 1: Visual images of the three formulations

Table 3: Organoleptic Analysis of the three formulations

Formulation	Appearance	Taste	Odor	Texture
A	Cloudy White	Hazelnut	Hazelnut	Gel substance
B	Dirty White	Peanut	Hazelnut	Oil
C	Light Yellow	Hazelnut	Hazelnut	Condensed liquid

pH

Formulation A has the lowest pH at 5.82, suggesting higher acidity, which enhances pharmaceutical elegance and potentially stabilizes the emulsion (Juttulapa et al., 2013). This acidity preserves emulsion integrity, reducing oil flocculation at the interface for more excellent stability. Formulation B has an average pH of 6.10, and Formulation C's average pH is 5.84.

Viscosity

Formulations A, B, and C, prepared at 25°C, displayed respective viscosities of 120 cP, 470 cP, and 957 cP. Viscosity is a key consumer-quality indicator, with thicker liquids often associated with higher perceived quality (Stribitcaia et al., 2022). The results demonstrated an inverse relationship between water content and viscosity, highlighting that lower water content correlates with higher viscosity and enhanced pharmaceutical elegance (Juntarasakul and Maneeintr, 2018). Notably, Formulation C had the highest viscosity and the least water content among the formulations.

Particle Size Distribution

The Particle Size Distribution (PSD) analysis for argan oil in three formulations revealed similar particle sizes within the curve (Figure 2). Formulation A had oil droplet sizes ranging from 0.58 µm to 116.21 µm, Formulation B ranged from 0.20 µm to 262.38 µm, and Formulation C ranged from 1.01 µm to

300.5 µm. Each formulation exhibited a distinct particle size distribution, evident in the two peaks on the graph, with smaller particles in the first peak and larger particles in the second. Formulation A had 13.17% small particles and 4% large particles, Formulation B had 7.34% small particles and 5.54% large particles, and Formulation C had 8.81% small particles and 3.90% large particles. The smaller particle size in Formulation A contributed to a larger surface area, enhancing protective film formation and pharmaceutical elegance (Gasparelo et al., 2022). Moreover, Formulation A's higher interfacial oil value also supported its pharmaceutical elegance, indicating a stronger integration of surface oil tension (Nam et al., 2021).

Oil-in-Water Emulsion Tests (Gravimetric & Dye Method)

In the gravimetric test, Formulation A retained an average of 0.89 grams of oil on the filter paper, Formulation B retained 1.20 grams, and Formulation C retained 1.50 grams. These results illustrate varying oil retention corresponding to the different volumes of Argan oil used in the samples.

For the dye method, Formulation A had fewer but larger globules than Formulation C, while Formulation B had smaller, more prominent globules. Formulation C exhibited the smallest droplet size and the highest globule count. The addition of water-soluble dye confirmed all three formulations (A, B, and C) as oil-in-water emulsions (Sarathchandraprakash et al., 2013). The retained oil on the filter paper during gravimetric analysis and the dye method further validated the presence of dispersed oil droplets within the continuous water phase of each formulation (Hu et al., 2017).

CONCLUSION

In summary, Formulation A demonstrated notable attributes, making it the optimal choice for the oil-in-water emulsion containing argan oil. Addressing compatibility concerns and assessing sensory attributes, pH levels, and particle size distribution successfully achieved the desired pharmaceutical elegance, laying a promising foundation for developing stable and effective oral emulsions.

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CONFLICT OF INTEREST

The authors declare that they have no known competing financial interests or personal relationships that could inappropriately influence the work reported in this paper.

CONTRIBUTIONS OF INDIVIDUAL AUTHORS

Led the research and provided overall guidance throughout the study: Mikaela Mae Suasin

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