Physicochemical evaluation of *Prinsepia utilis* seed oil (PUSO) and its utilization as a base in pharmaceutical soap formulation

Jitendra Pandey[1#*], Srijana Acharya[1#], Rakshya Bagale[1], Akriti Gupta[1], Pooja Chaudhary[1], Bikash Rokaya[1], Manju K.C.[1], Pramod Aryal[1,2], Hari Prasad Devkota[3–5]

[1]Department of Pharmacy, Crimson College of Technology, Affiliated to Pokhara University, Devinagar, Butwal, Nepal; [2]Department of Biochemistry and Molecular Biology, Monash University, Clayton, Australia; [3]Graduate School of Pharmaceutical Sciences, Kumamoto University, Chuo-ku, Kumamoto, Japan; [4]Headquarters for Admissions and Education, Kumamoto University, Kurokami, Chuo-ku, Kumamoto, Japan; [5]Pharmacy Program, Gandaki University, Pokhara, Nepal

[#]These authors are the first authors of this research.

[*]**Corresponding Author**: Jitendra Pandey, Department of Pharmacy, Crimson College of Technology, Affiliated to Pokhara University, Devinagar, Butwal, Nepal. Email: jitupandey01301@gmail.com

Received: 19 August 2022; Accepted: 3 April 2023; Published: 19 April 2023

RESEARCH ARTICLE

Abstract

This study aims to evaluate the standard physicochemical parameters, such as iodine value, acid value, saponification value, ester value, refractive index, peroxide value, and viscosity, of *Prinsepia utilis* (*P. utilis*) seed oil (PUSO) obtained as hexane extract from seeds, and to formulate ketoconazole soap (2% w/w) by using extracted oil as a base. The quality control standards of the final ketoconazole soap complied with the standards specified in Indian Pharmacopeia. Pharmaceutical soap was obtained by treating PUSO with potassium hydroxide (KOH), undergoing basic saponification. All physicochemical parameters, such as acid value (21.78 mg KOH/g), saponification value (194.13 mg KOH/g), iodine value (99.7 g I_2/100 g), ester value (172.35 mg KOH/g), refractive index (1.464), and viscosity (192 centipoises [cps]), conformed to industrial standards, except the peroxide value (19.23 milliequivalent KOH/g). Besides, evaluation of quality control parameters of pharmaceutical soap suggested that its various parameters, such as pH (7.3), foam-forming ability (14.5 cm), foam retention time (15 min), total fatty matter (69.31%), moisture content (10.35%), and drug content (99.37%), were within the acceptable limit. Overall, our study showed that *P. utilis* base was physicochemically stable and suitable for manufacturing cosmetic products, soaps, and shampoo in an economical manner, rather than using expensive chemical additives, in the pharmaceutical and cosmeceutical industry. Further, this study suggested that therapeutically and commercially successful ketoconazole soap, with all the required quality control parameters, could be manufactured by using naturally available oil at a low cost.

Keywords: ketoconazole; physicochemical parameters; *P. utilis*; PUSO; fixed oil; soap formulation

Introduction

Prinsepia utilis Royle (Family: Rosaceae) is a bushy deciduous shrub having a height of about 1.5–3 m. The plant is a native of the Himalayan region, widely distributed in Nepal, Bhutan, China, India, Bangladesh, and Pakistan, up to an altitude of 1600–3000 m (Gupta *et al.*, 2015; Kunwar and Duwadi, 2003; Watanabe *et al.*, 2013, Zheng *et al.*, 2022). Locally known as "Dhatelo" or "Gotyalo" in Nepal (Gupta *et al.*, 2015), the plant is distributed at an

ISSN 1757-837X online, DOI 10.15586/qas.v15i2.1176

high altitude of 1800–3000 m in central and western districts of Nepal, such as Makawanpur, Myagdi, Kalikot, Humla, Jumla, Mugu, Dadeldhura, and Jajarokot (Bagale *et al.*, 2022; Bhattarai *et al.*, 1992; Kewlani *et al.*, 2022a, 2022b; Kunwar and Duwadi, 2003; Manandhar, 1986, 1995; Watanabe *et al.*, 2013). Different parts of this plant have been used traditionally, mainly for food and medicinal purposes, by the people of Nepal, India, and China (Gupta *et al.*, 2015; Guan *et al.*, 2014; Manandhar, 1986). The root bark is used for stomach disorders in the far western regions of Nepal (Kunwar and Duwadi, 2003).

The indigenous population of Nepal have traditionally considered the seeds of this plant as a nutritional food material and a useful source of oil extraction (Bagale *et al.*, 2022; Bhattarai *et al.*, 1992; Kewlani *et al.*, 2022b) The most relevant part of the plant is its seeds, which contain about 37.2% fat and its oil is used as a vegetable oil as well as massage oil for rheumatism, headache, acne, and boils. The seed oil is a very useful natural emollient for cracked feet and hands in the winter season. In Nepal, it has been utilized as butter for oil lamps and hair oil (Watanabe *et al.*, 2013). The people of the Jumla district of Nepal use seed oil residue to cure eczema or ringworm as well as to wash clothes (Watanabe *et al.*, 2013). The seed oil is considered as a suitable source of hydrogenation and soap formulation (Bagale *et al.*, 2022; Kewlani *et al.*, 2022b; Maikhuri *et al.*, 1994). Warm seed oil is reported as an effective therapy to treat body ache caused by heavy physical load (Manandhar, 1995; Zheng *et al.*, 2022).

Besides, seed oil and leaves of *P. utilis* are extensively used in Indian and Chinese folk medicine to treat arthritis, bone disorders, joint ailments, blood pressure, and atherosclerosis (Gupta *et al.*, 2015; Zhang *et al.*, 2018). Diverse bioactive compounds, such as diterpenoid glucosides, hydroxynitrile glucosides, rutin, isorhamnetin-3-O-rutinoside, cyanidin-3-O-rutinoside, quercetin-3-O-glucoside, triterpenoids, etc., are reportedly found in the seeds (Zhang *et al.*, 2018). In addition, *P. utilis* seeds contain a rich amount of fixed oils.

In spite of the increasing demand for preparing cleansing formulations, most of the commercially available cleansing preparations have various difficulties, such as chemical instability of the base, necessity of many pharmaceutical excipients to ensure base stability, high cost of production of synthetic base, and hypersensitivity of the base to the skin. In the current scenario, numerous industries and research organizations are exploring the possible pharmacological, nutritional, and cosmeceutical applications of different fixed oils isolated from natural sources such plants, herbs, and seeds. Consequently, underused seed oil is successfully utilized for the commercial production of effective cosmetic items (Atolani *et al.*, 2020), such as creams, soaps, shampoo, skin care products, toothpaste, beauty products, hair conditioners, deodorants, and hair care products (Tareau *et al.*, 2017).

Although, plain or antimicrobial commercial soaps, prepared by incorporating synthetic agents, are successful to achieve desired cleansing and disease-combating effects, these products are also responsible for several adverse reactions, such as dryness of skin, damage to skin integrity, browning of hair, skin eruptions, irritation, brittle hair, etc. Different synthetic antioxidant agents used in soaps, such as butylated hydroxytoluene, butylated hydroxyanisole, and paraben derivatives, potentially induce allergic reactions and are possible carcinogens (Atolani *et al.*, 2016; Nowak *et al.*, 2018). Similarly, the widely used synthetic antimicrobial agents (such as triclosan) in soaps are toxic cancer-causing agents.

Besides, other synthetic additives, such as fragrances, lathering agents, preservatives, and colorants, are also considered as potential threats to human health (Gultekin *et al.*, 2006; Nowak *et al.*, 2018). On the other hand, the preparation of natural or organic soaps involves the incorporation of natural fixed oils and other natural additives, such as honey, essential oils, plant-derived fragrances and colorants, antimicrobial plant extracts, vitamins, and natural antioxidants (polyphenols, such as flavonoids and phenolic acids). Therefore, these soaps fascinate to have several benefits, such as moisturizing, skin smoothing, antimicrobial, anti-inflammatory, antiviral, wound-healing, and anti-aging properties (Aburjai and Natsheh, 2003; Bansal *et al.*, 2005). Therefore, many researchers are exploring the potential of sustainable natural sources as a base (Kim *et al.*, 2015). Thus, among different natural sources, oils from the seeds of various edible plant species could be the best alternative.

The skin is the largest exposed organ of the human body. It is highly prone to diverse harmful materials that could induce various skin-related pathological conditions. Therefore, maintaining hygiene and neatness is necessary for the protection of the skin from different possible disorders associated with microbial infections. Thus, use of soaps is an easy and effective way to remove all harmful foreign particles. Appropriate use of the soaps ensures effective cleansing, as it obliterates different microorganisms, for instance, *Pseudomonas species*, *Klebsiella pneumoniae*, *Staphylococcus aureus*, and *Proteus vulgaris*, which are main causative agents for various skin infections (Sindhu *et al.*, 2019).

The ever-increasing demand of consumers to use cleansing agents has prompted researchers to innovate different types of soap products in terms of quality, quantity, and function (Antonić *et al.*, 2020; Widyaningsih *et al.*, 2018).

In the present scenario, the soap industry is developing a variety of antibacterial and antifungal soaps containing active antimicrobial ingredients (Kim *et al.*, 2015; Yu *et al.*, 2018). In the form of topical formulations, various preparations, such as ointments, creams, gels, shampoos, soaps, and powders, are available commercially (Shirsand *et al.*, 2012).

Ketoconazole is one of the potent broad-spectrum antifungal drug belonging to the synthetic imidazole group (Rane and Padmaja, 2012; Staub *et al.*, 2010). The drug has a significant therapeutic effect against systemic and superficial mycosis, along with candidiasis, malassezia, and dermatophytoses (Choi *et al.*, 2019; Shirsand *et al.*, 2012). It inhibits the synthesis of fungal ergosterol, a key constituent of fungal cell membrane, and results in cell death. Likewise, it also interferes with the biosynthesis of fungal phospholipids, triglycerides, and oxidative enzymes, thereby increasing the cellular concentration of toxic hydrogen peroxide. In treating *Candida albicans* infection, it prevents the formation of invasive mycelia from blastospores (Winnicka *et al.*, 2019). Ketoconazole soap is the most popular and convenient cosmetic product used extensively for the treatment of fungal and yeast infections of the skin. Several skin-related developments, such as seborrhoeic dermatitis (Dreno *et al.*, 2003), pityriasis versicolor, dermatophytoses, candida infections, androgenetic alopecia, leishmaniasis, superficial dermatomycosis, and yeast-induced blepharitis (Choi *et al.*, 2019), have been successfully treated by using ketoconazole soap.

Prinsepia utilis seed oil has a long history of ethnomedicinal and economic usage by different ethnic groups in Nepal. However, no scientific studies have been conducted on the physiochemical properties, and the possible pharmaceutical and cosmeceutical applications of PUSO. Hence, this study aimed to evaluate the physicochemical parameters (pH, specific gravity, refractive index, melting point, viscosity, acid value, iodine value, saponification value, peroxide value, and ester value) and to formulate 2% w/w ketoconazole soap by using PUSO as a soap base along with its quality control analysis.

Materials and Methods

Chemicals and solvents

Standard ketoconazole powder was obtained from Biogain Remedies, Butwal, Nepal. Similarly, iodine trichloride, sodium thiosulphate, potassium iodide, and potassium bromate iodine were obtained from Merck India. Furthermore, mercuric iodide and iodine monobromide were obtained from Thermo Fischer Scientific, India.

Instruments

The following instruments were used in the study: Brookfield viscometer (Brookfield AMETEK, DV plus model, Boulevard Middleboro, USA), digital balance (ATX224, SHIMADZU Corporation, Manila, Philippines), hot air oven (S.M. Scientific Instruments, New Delhi, India), rotary evaporator (R-210/215, BUCHI Labor Technok AG, Flawil, Switzerland), UV spectrophotometer (UV-1800 model; Shimdazu Corporation, Shanghai, China), sonicator (INDOSATI Scientific Lab Equipments, Haryana, India), Abbe refractometer RFT-A1 (Toledo, OH, USA), and PC9500 benchtop digital pH meter, (Columbus, Ohio, USA).

Extraction of seed oil

Ripened fruit of *P. utilis* were collected from Khalanga-1, Jumla district, Nepal (a temperate region, 2518 m above sea level) in November 2020. The collected plant material was identified and authenticated by National Herbarium and Plant Laboratory Godawari, Nepal (Letter No. 078/079). The pulp of collected fruit was separated from hard seeds. Seed kernels were removed from hard shells and dried on clean filter papers in a well-ventilated laboratory room at 25°C for 2 weeks.

Dried seed kernels were comminuted using a grinder and a sticky coarse powder was obtained for the presence of oil content. The coarse powder was then subjected to extraction by applying cold maceration method, in which 100-g dried powder was soaked in 500 mL of hexane in conical flasks with occasional shaking for 2 days. The menstrum was strained, and the marcs were pressed and filtered. The process was repeated for three times. The filtrate was collected and dried with the help of a rotatory vacuum evaporator at 40°C to obtain orange color liquid hexane extract in the form of PUSO. The extract was again dried in a vacuum desicator for a few days and stored at 4°C for further use. The photographs of collected fruits, dried seeds, seed kernels, and hexane extract (oil) of *P. utilis* are shown in Figure 1.

Physiochemical evaluation of PUSO

The physicochemical analysis was carried out in accordance with the Indian Pharmacopeia (Vol 1; Government of India, 2018) and relevant literature (Pandey *et al.*, 2021). All the experiments were conducted in triplicate.

Acid value

Approximately 20 g of PUSO was dissolved in 100 mL of neutralized mixture of ether and 95% ethanol (1:1 v/v).

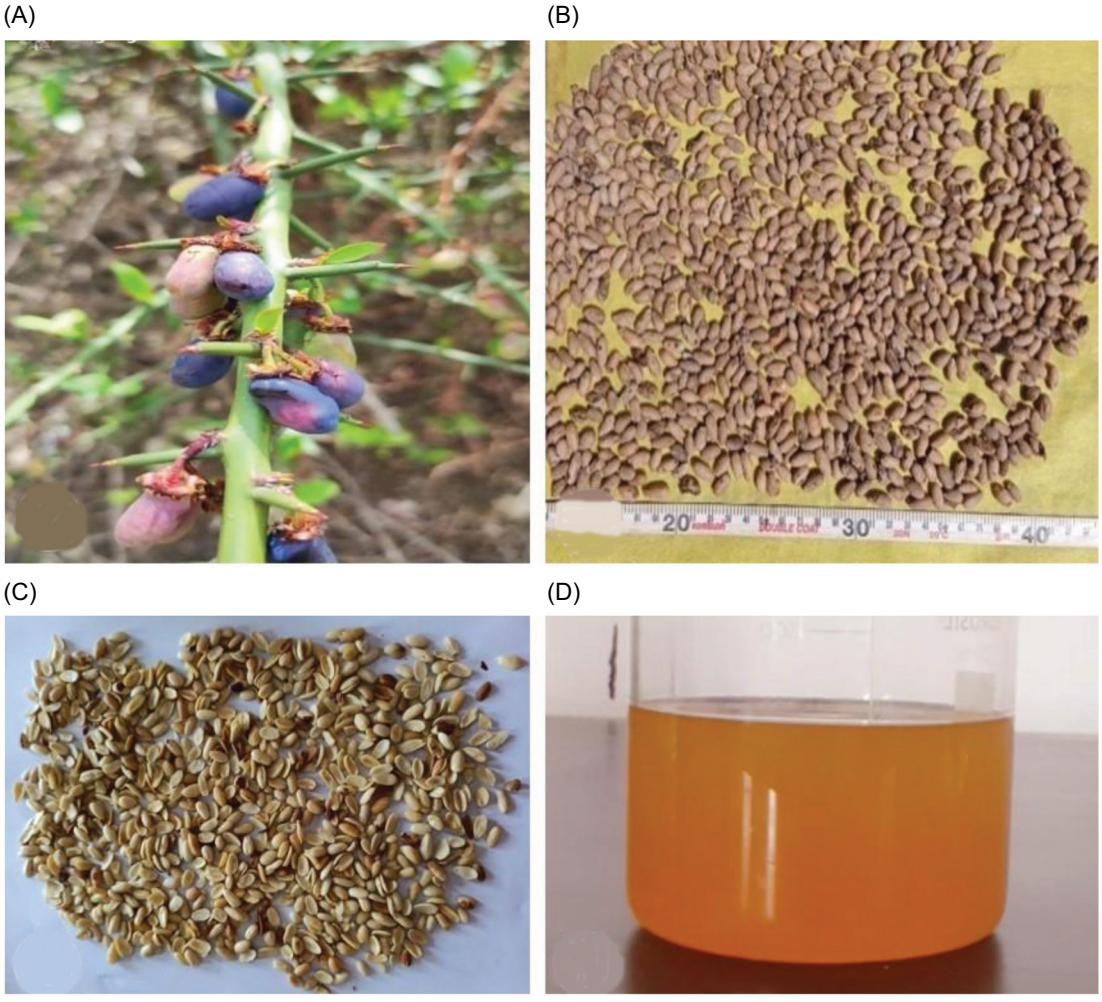

Figure 1. Photographs of *P. utilis* (A) ripen fruits, (B) dried seeds, (C) dried seed kernels, and (D) hexane extract (PUSO).

The titration was fulfilled between the sample solution and the standardized potassium hydroxide (KOH) to determine acid value by using Equation 1 (Pandey *et al.*, 2020):

$$\text{Acid value} = \frac{5.61n}{w} \quad (1)$$

where n is the volume of 0.1-M KOH reacted and w is the weight of the sample used for evaluation.

Iodine value

The iodine value was calculated by adopting the Hanus method (Pandey *et al.*, 2020). At the beginning, 290 g of sample was mixed with 15 mL of chloroform in a 300-mL dry iodine flask. Then, 25 mL of iodine monobromide solution was poured gently from the burette. The sample mixture was incubated for 30 min at a dark place with occasional shaking. Then, 100 mL of distilled water and 10 mL of 30% w/v of potassium iodide solution were added. After incubation, the sample mixture was titrated with a standardized solution of 0.1-M sodium thiosulphate, in which starch solution was used as an indicator at the end of titration. The volume of 0.1-M thiosulphate (mL) reacted was determined as "x" value. The same titration process was repeated without using the sample and volume consumed (mL) was observed as "y" value. Finally, the iodine value was determined by using Equation 2:

$$\text{Iodine value} = 1.269\ (y - x)/w \quad (2)$$

where w is the weight of the sample (g) used for evaluation.

Saponification value

Tentatively 2 g of PUSO was placed in a 250-mL round bottom flask connected to a reflux condenser. Then, a small amount of pumice powder and 25 mL of ethanolic

0.5-M KOH were added and boiled in a water bath for 30 min. After cooling of the sample for a few minutes, it was titrated against 0.5-M HCl by adding phenolphthalein. Blank titration was also carried out without adding the sample. The saponification value was determined using Equation 3 (Pandey *et al.*, 2020):

$$\text{Saponification value} = 28.5\ (y - x)/w \quad (3)$$

where w is the weight of the sample (g) used for evaluation; x and y are the volume of HCl (mL) consumed by the sample solution and the blank solution, respectively.

Peroxide value

About 5 g of the test sample was added in a 250-mL conical flask, having a glass stopper. A mixture of glacial acetic acid and chloroform (3:2 ratio) was poured slowly with continuous shaking, followed by the addition of 0.5 mL of saturated potassium iodide. The homogenous sample mixture was then kept for 1 min, with frequent shaking. Then, 20 mL of distilled water was mixed and the titration of the obtained sample mixture was performed against a standardized solution of 0.01-M sodium thiosulphate until the disappearance of yellow color. In addition, 0.5 mL of 5% w/v starch solution was put dropwise and titration was continued with vigorous shaking until the disappearance of blue color ("x" in mL). In the same manner, blank titration was performed without sample ("y" in mL). Finally, the peroxide value was determined by using Equation 4 (Pandey *et al.*, 2020):

$$\text{Peroxide value} = 10(x - y)/w \quad (4)$$

where w is the weight of the sample (g) used for evaluation.

Ester value

Ester value of the sample was determined by using Equation 5 (Pandey *et al.*, 2020):

$$\text{Ester value} = \text{Sponification value} - \text{Acid value} \quad (5)$$

Determination of specific gravity

At first, a clean and dried pycnometer, having a 50-mL capacity, was weighed along with its cap, noted as "a." Then, the pycnometer was filled with samples until it was overflowed, closed with a stopper, and weighed again with contents and noted as "b." After cleaning and drying, the same pycnometer was filled with water and weighed, recorded as "c." Finally, the specific gravity was calculated using Equation 6 (Muhammad *et al.*, 2013):

$$\text{Specific gravity} = \frac{b - a}{c - a} \quad (6)$$

Measurement of pH and refractive index

For measuring pH, 100 mL of oil was poured in a clean and dry beaker. The pH was measured thrice by using a digital pH meter. The refractive index was determined at room temperature with the help of Abbey refractometer (Muhammad *et al.*, 2013; Pandey *et al.*, 2020).

Measurement of viscosity

For measuring the viscosity of PUSO, a DV-III ULTRA Brookfield viscometer was used. For this, approximately 20 g of oil was poured in a dry 250-mL beaker. Viscosity was determined by using spindle No. 64. The test sample was subjected to rotation for 1 min at 10 rpm with 16.1 dyne-cm torque. The operation was carried out at a temperature of 25°C. The experiment was conducted thrice and the data was presented in centipoises (cps) (IP, Vol 1, Government of India, 2018; Mekkawy *et al.*, 2013; Pandey *et al.*, 2021).

Formulation of 2% w/w ketoconazole soap

Soap was developed using basic saponification reaction; in which natural PUSO was reacted with KOH to produce soap. For this, 100 g of PUSO was taken in a beaker and heated in a water bath at 55°C. In another beaker, 19.413-g KOH required to saponify 100-g oil was dissolved in an optimum volume of deionized water and allowed to cool to 35–40°C. Then, both solutions were mixed with continuous stirring for about 30 min, until the oil is completely converted into a homogenous solution. The solution was cooled followed by filtration using Buchner funnel and Whatman filter paper No. 1. After that, 300 mL of saturated sodium chloride solution was poured into the filtrate to precipitate the soap. The precipitate was removed and kept in a clean beaker. To prepare 25-g medicated soap, 24.5-g soap and 0.5-g ketoconazole were mixed with mild heating and continuous stirring for 20 min. Finally, the product was poured in a suitable mold and allowed to solidify for a few hours to get the desired medicated soap (Ruckmani *et al.*, 2014; Touré *et al.*, 2010).

Evaluation of 2 % w/w ketoconazole soap

pH measurement

Aqueous solution, 100 mL and 10% w/v, was used to measure pH by using digital pH meter (Pandey *et al.*, 2021; Sindhu *et al.*, 2019).

Foam-forming ability

Exactly 1-g soap was dissolved in about 50-mL water in a 100-mL graduated measuring cylinder, shaken for about 2–3 min and allowed to stand for 10 min. Then, the height of the foam formed was measured by using a measuring scale (Sindhu *et al.*, 2019).

Drug content

Initially, grinding of 10 pieces of soap (length, 4.7 cm, width, 2.12 cm, height, 0.78 cm, and weight, 25 g) was done in a pestle and mortar to prepare infinitesimal pieces. Then, 2.5 g of sample and 50 mg of ketoconazole were mixed in a 100-mL dry volumetric flask and dissolved with methanol. The sample solution was sonicated for 30 min to ensure complete solubilization of ketoconazole. After filtration, the sample was diluted to have the final solution of 25 parts per million (ppm). Similarly, the standard solution was also prepared by taking 50 mg of ketoconazole standard in a 100-mL volumetric flask dissolved with methanol. With proper dilution, a standard ketoconazole solution of 25 ppm concentration was prepared. Thus, both sample and ketoconazole solution were analyzed at 240 nm using a UV-visible spectrophotometer (Naveed and Jaweed, 2014). Content of the drug was determined by using pharmacopeial method with the help of Equation 7 (Dhakal *et al.*, 2022; Koirala *et al.*, 2021; Naveed and Jaweed, 2014; Pandey *et al.*, 2020):

$$\frac{\text{Absorbance of sp}}{\text{Absorbance of std}} \times \frac{\text{Wstd}}{100} \times \frac{5}{100} \times \frac{100}{\text{Wsp}} \times \frac{100}{5} \times \frac{\text{Purity of std}}{100} \times \frac{(100 - \text{LOD})}{100} \times 100 \quad (7)$$

where sp is the sample, std denotes the standard solution, Wsp is weight of the sample ointment taken (2.5 g), Wstd is weight of the standard drug taken (50 mg), and LOD is loss on drying of the standard.

Determination of moisture content

At first, a dried clean crucible was weighed, "a," and tarred. Then, about 6 g of soap was weighed, "b." The crucible content was then heated for 2 h at a temperature of 101°C. After that, the crucible was kept inside a desicator and cooled. Finally, the weight of crucible containing sample was noted, which is "c." The moisture content was calculated by using Equation 8 (Sindhu *et al.*, 2019):

$$\text{Moisture content} = \frac{b - (c - a)}{b} \times 100 \quad (8)$$

Determination of total fatty matter (TFM)

About 10-g soap (W) was dissolved in 150-mL distilled water. The solution was mixed with 20% sulfuric acid and heated until a clear solution is obtained. After few minutes, a thick film of fatty acid appeared on the surface of the solution. Then, about 7 g of wax (X) was added to the solution and heated. A cake was formed (Figure 2C) on cooling, which was removed and weighed (A). Finally, TFM was calculated by using Equation 9 (Sindhu *et al.*, 2019):

$$\% \text{ Total Fatty Matter} = \frac{(A - X)}{W} \times 100 \quad (9)$$

Results and Discussion

Yield of *P. utilis* seed extract

The yield of *P. utilis* seed hexanolic extract was found as 26.43%. Previous studies have reported extractive yield for some of the commercial oils, such as olive oil (14%; Abenoza *et al.*, 2013), coconut oil (61.3%; Famurewa *et al.*, 2021), and palm oil (59.32%; Teixeira *et al.*, 2013). This demonstrates the moderate yield of PUSO.

Physicochemical analysis of PUSO

Different physicochemical properties of PUSO were analyzed for the characterization of its quality and condition. Table 1 shows the comparison of physicochemical parameters of PUSO with olive oil (Muhammad *et al.*, 2013) and *Diploknema butyracea* (Roxburgh) seed fat (chyuri fat; Krist, 2020; Pandey *et al.*, 2021). The oil was orange yellow in color (Figure 1D). The acid value of PUSO was higher than that of olive oil, which indicated the presence of higher proportion of free fatty acids in the sample. However, it had a lower acid value, compared to chyuri fat.

The acid value signifies the susceptibility of oil toward triglyceride degradation because of temperature, light, cold, and lipase enzyme activity (Inekwe *et al.*, 2012;

Table 1. Results of physicochemical parameters of PUSO, compared to olive oil and chyuri fat.

Parameters	Samples		
	PUSO	Olive oil	Chyuri fat
Acid value (mg KOH/g)	21.78 ± 1.76	4.53	61.86 ± 1.16
Iodine value (g I_2/100 g)	101.14 ± 2.54	76	36.26 ± 0.89
Peroxide value (Meq KOH/g)	19.23 ± 0.34	17	3.14 ± 0.17
Saponification value (mg KOH/g)	194.13 ± 2.87	186.33	225.05 ± 1.98
Ester value (mg KOH/g)	172.35 ± 1.76	181.77	163.19 ± 2.75
Viscosity(centipoise)	192 ± 2.16	62	310 ± 0.61
pH	5.81 ± 0.31		
Refractive index	1.46 ± 0.08	1.46	1.45–1.46
Specific gravity (g/mL)	0.89 ± 0.12	0.91	0.92

Oladiji *et al.*, 2010; Pandey *et al.*, 2021). Besides this, acid value demonstrates the suitability of oil for edible purposes. Any oil or fat having an acid value higher than 4 mg/g is considered unhealthy for edible purposes (Amoo *et al.*, 2004). Thus, the acid value of date oil suggests that its consumption could be harmful for human consumption.

The higher iodine value signifies that the proportion of unsaturated fatty acids is high. Determination of iodine value is helpful to identify the proportion of double bonds, which are prone to oxidative degradation, in oil sample (Bello *et al.*, 2011). The higher value of iodine in PUSO (98.89 g I_2/100 g) indicated that it contained a higher proportion of unsaturated fatty acids. Main fatty acids found in PUSO are ester polyunsaturated oleic acid (28.9%), monounsaturated linoleic acid (16.4%), vaccenic acid (11%), saturated stearic acid (11.4%), and saturated palmitic acid (22.1%). Overall, the amount of unsaturated fatty acids found in PUSO was 65.2% (Kewlani *et al.*, 2022b; Maikhuri *et al.*, 1994; Yang *et al.*, 2012).

It has been reported that oil or fat samples having iodine value lower than 100 g I_2/100 g are considered stable chemically for industrial purposes (Chinedu *et al.*, 2017), such as cosmeceutical industry, margarine production, bakery production, and drug industry (Samuel *et al.*, 2017). The low iodine value of any oil or fat indicates its chemical stability against rancidity and oxidation of products manufactured (Chinedu *et al.*, 2017; Samuel *et al.*, 2017). The iodine value of PUSO was almost similar to that of edible sesame oil (Yermanos *et al.*, 1972).

The stability of oil or fat against possible rancidity could be correlated with its peroxide value, which indicates possible auto-oxidation (Chinedu *et al.*, 2017). Oil or fat having a peroxide value higher than 10 meq/kg is susceptible to auto-oxidation because of peroxidase and lipoxygenase enzymes if moisture content or other trace elements are present (Bello *et al.*, 2011; Chinedu *et al.*, 2017). The higher peroxide value of PUSO indicated its susceptibility toward peroxidation (Aremu and Akinwumi, 2014). Generally, unrefined oil has a comparatively higher peroxide value than refined oil. This could be a possible reason for higher peroxide value of PUSO (Aremu and Akinwumi, 2014). Therefore, comparative study of different extraction techniques for PUSO could be a significant scientific investigation to improve its peroxidation value.

The saponification value of oil or fat indicates the type of fatty acid present in terms of molecular weight. If any oil/fat sample has a low saponification value, then the sample contains a higher amount of fatty acids having high molecular weight. The higher saponification and ester values of PUSO indicated that it contained a greater amount of lower molecular weight short-chain and easily saponifiable triglycerides. These types of oils are suitable candidates for pharmaceutical, cosmeceutical and related industrial purposes (Bello *et al.*, 2011; Inekwe *et al.*, 2012). PUSO had higher saponification value (194.13), compared to commercially utilized oils, such as palm oil (192.64; Udensi and Iroegbu, 2007), olive oil (186.33; Muhammad *et al.*, 2013), and sunflower oil (182.23; Alibe and Inuwa, 2012).

Specific gravity of any oil/fat sample represents its one of the most significant quality control parameters. Adulteration of an expensive oil sample by cheaper oil alters the specific gravity of the sample oil. Thus, specific gravity is a useful indicative parameter to check the quality of any oil sample (Yadav, 2018). In the present study, the specific gravity of PUSO was 0.89 g/mL, which was almost similar to that of olive oil (0.91 g/mL; Nierat *et al.*, 2014).

The refractive index of oil correlates with its possible rancidity. It has been proved that oil with a higher refractive index has a greater chance of rancidity (Arya *et al.*, 1969). In this study, refractive index of PUSO (1.464) was found similar to that of pumpkin oil (1.465; Alfawaz *et al.*, 2004)

but higher than that of olive oil (1.46; Muhammad *et al.*, 2013). In addition, oil samples having a refractive index in the range of 1.475–1.485 are classified as drying oil (Aremu *et al.*, 2006). In other terms, oil sample having an iodine value lower than 115 g I_2/100 g is classified as non-drying oil. Thus, it can be concluded that PUSO was a non-drying type of oil. These oil types do not form layer when having contact with air, and their chemical stability is always higher than that of drying oil (Islam *et al.*, 2014).

In addition, PUSO had higher viscosity, compared to other common oil samples, such as pumpkin oil (48.09 cp; Alfawaz *et al.*, 2004) and olive oil (84 cp; Nierat *et al.*, 2014). Oil samples with higher viscosity are suitable for lubrication purposes (Nierat *et al.*, 2014).

Evaluation of 2% w/w ketoconazole soap

After ensuring chemical suitability of PUSO as a soap base, 25 g of 2% w/w ketoconazole soap (Figure 2A) was formulated by basic saponification method. As shown in Table 2, various quality control parameters, namely pH, foam-forming ability, moisture content, TFM, and drug content, were determined. All the measured parameters were found within the limits as specified by the pharmacopeia and literature.

Table 2. Results of different quality control parameters of 2% w/w ketoconazole soap formulated by using PUSO as a base.

Evaluation	Result
pH	7.3
Foam-forming ability(cm)	14.5 ± 0.5
Foam retention time (minutes)	15 ± 0.76
Determination of moisture content (%)	10.35 ± 0.25
Determination of TFM (%)	69.31 ± 1.72
Soap assay (%)	99.37 ± 1.02

pH of soap

The pH of ketoconazole soap was optimal for the human skin. It is reported that pH of 5.5–7.5 is normal for the human skin (Sindhu *et al.*, 2019).

Foam-forming ability

The foaming index of the formulation was 14.5±0.5 cm, while the foam retention time was 15 min. Compared with other soaps, we concluded that the foam-producing ability of the soap was satisfactory and stable (Akuaden *et al.*, 2019; Jagdale *et al.*, 2011). Figure 2B shows the foam-forming ability of newly formulated 2% w/w ketoconazole soap.

Moisture content

Total moisture content predicts the shelf life of any soap. If the moisture content of soap is in excess, even in normal storage conditions, water present in it could react with unsaponified oil or fat to liberate glycerol and free fatty acids because of hydrolysis. According to the Encyclopedia of Industrial Chemical Analysis, normal range of moisture content for any soap is 10–15% (Akuaden *et al.*, 2019). Thus, the newly formulated ketoconazole soap demonstrated satisfactory results in terms of moisture content (10.35%).

Total fatty matter

Determination of TFM (Figure 2C) is one of the significant parameters to ensure the quality of any soap. TFM demonstrates the extent of moisturizing effect produced by soap when applied to the skin. If the TFM of soap is

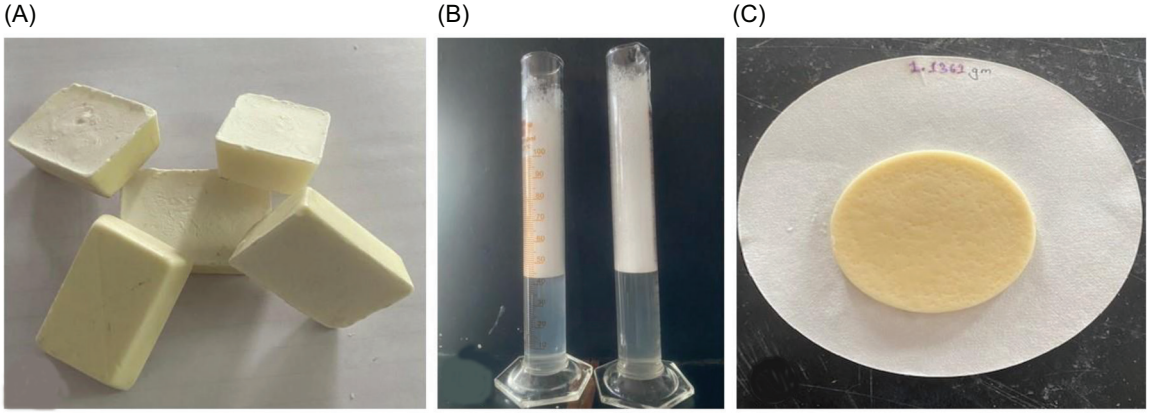

Figure 2. Photographs of ketoconazole soap (2% w/w) formulated by using (A) PUSO oil as a base, (B) foam-forming ability shown by newly formulated PUSO-based soap, and (C) total fatty matter present in the soap.

lower, it may increase the dryness of the skin (Ahmed *et al.*, 2021; Akuaden *et al.*, 2019; Jagdale *et al.*, 2011). Based on the TFM value, soaps are classified into different grades. Soaps having TFM above 76% are categorized as Grade 1 soap whereas the TFM limit for Grade 2 soap is 60–70% (Ahmed *et al.*, 2021). The TFM of PUSO-based soap was 69.31%, thus insuring it a Grade 2 category, and was compared to some commercially available soaps such as Lifebuoy (63.4%; Mwanza and Zombe, 2020; Sindhu *et al.*, 2019), Lux Beauty (60.7%; Sharma *et al.*, 2020), Dettol (65.4%; Mwanza and Zombe, 2020), and Liril Lime and Tea Tree Oil soap (70.4%; Sharma *et al.*, 2020).

Drug content in the soap

The pharmacopeial assay was performed to quantify the amount of active ketoconazole present in the soap, and it was found within the limits (95–105%), as specified by the US Pharmacopeia 2020 (USP 2A; pp. 2506–2507). Therefore, commercial manufacturing of a medicated soap by using PUSO as a base could be a useful alternative. However, extensive studies regarding various parameters, such as real-time stability, accelerated stability, skin irritation test, drug release profile of the soap, and microbial studies, are important to ensure commercial acceptability of the soap.

Conclusions

This study examined various physicochemical parameters (iodine, acid, peroxide, saponification, and ester values, viscosity, pH, and refractive index) of PUSO and concluded that that it was suitable for pharmaceutical, cosmeceutical, and related industrial purposes. However, its high acid value signified that it is not suitable for human consumption as a food material. In addition, the peroxide value of PUSO could be minimized by its lead purification.

The antifungal soap prepared by using PUSO only demonstrated acceptable results, related to its chemical and physical stability. Different quality control parameters, namely pH, foam height, foam retention time, TFM, and drug content, were within the acceptable limits and comparable to several Grade 2 marketed soaps. The antifungal soap prepared by using natural oil only may show several beneficial effects, such as moisturizing, antioxidant, antiseptic, and skin soothing effects, rejuvenation of hair and skin, and no risk of carcinogenicity as observed in synthetic soaps. Therefore, further investigation is required so that PUSO could be commercialized as a suitable alternative for other synthetic oil or fat samples. Moreover, commercialization of PUSO could benefit economically the local communities involved in the cultivation and collection of *P. utilis*.

Data Availability

All the data used to support the results of this research are available in this manuscript.

Author Contributions

Jitendra Pandey conceived and designed the experiment. Srijana Acharya, Rakshya Bagale, Jitendra Pandey, Pooja Chaudhary, Akriti Gupta, and Bikash Rokaya performed the experiment. Jitendra Pandey analyzed the data and wrote the manuscript. Jitendra Pandey, Hari Prasad Devkota, Pramod Aryal, and Manju K.C. revised the final manuscript.

Funding

This research did not receive any funding but was performed as part of the partial fulfillment of an academic degree at Crimson College of Technology, affiliated to Pokhara University, Nepal.

Conflict of Interest

The authors declare no conflict of interest with respect to research, authorship, and/or publication of this article.

Acknowledgments

The authors are grateful to the students and staff of Department of Pharmacy, Crimson College of Technology for their technical support.

References

Abenoza M., Benito M., Saldaña G., Álvarez I., Raso J. and Sánchez-Gimeno A.C., 2013. Effects of pulsed electric field on yield extraction and quality of olive oil. Food and Bioprocess Technology 6: 1367–1373. https://doi.org/10.1007/s11947-012-0817-6

Aburjai T. and Natsheh F.M., 2003. Plants used in cosmetics. Phytotherapy Research 9: 987–1000. https://doi.org/10.1002/ptr.1363

Ahmed L., Hazarika M.U. and Sarma D., 2021. Formulation and evaluation of an ayurvedic bath soap containing extracts of three ayurvedic herbs. Journal of Medicinal Plants 9(2): 115–117.

Akuaden N.J., Chindo I.Y. and Ogboji J., 2019. Formulation, physicochemical and antifungal evaluation of herbal soaps of azadiractaindica and ziziphusmauritiana. IOSR Journal of Applied Chemistry 8: 26–34.

Alfawaz M.A., 2004. Chemical composition and oil characteristics of pumpkin (Cucurbita maxima) seed kernels. Food Science and Agricultural Research 129: 5–18.

Alibe I.M. and Inuwa B., 2012. Physicochemical and anti-microbial properties of sunflower (Helianthus annuus L.) seed oil. International Journal of Science and Technology 4: 151–154.

Amoo I.A., Eleyinmi A.F., Ilelaboye N.O.A. and Akoja S.S., 2004. Characterisation of oil extracted from gourd (Cucurbita maxima) seed. Journal of Food, Agriculture and Environment 2(2): 38–39.

Antonić B., Dordević D., Jančíková S., Tremlova B. and Kushkevych I., 2020. Physicochemical characterization of home-made soap from waste-used frying oils. Processes 8(10): 1219. https://doi.org/10.3390/pr8101219

Sustainable ChemistryPharmacyAremu M.O. and Akinwumi O.D., 2014. Extraction, compositional and physicochemical characteristics of cashew Anarcadiumoccidentale nuts reject oil. Asian Journal of Applied Science and Engineering 3(2): 227–234. https://doi.org/10.15590/ajase/2014/v3i7/5357

Aremu M.O., Olonisakin A., Bako D.A. and Madu P.C., 2006. Compositional studies and physicochemical characteristics of cashew nut (Anarcadiumoccidentale) flour. Pakistan Journal of Nutrition 5(4): 328–333. https://doi.org/10.3923/pjn.2006.328.333

Arya S.S., Ramanujam S. and Vijayaraghavan P.K., 1969. Refractive index as an objective method for evaluation of rancidity in edible oils and fats. Journal of American Oil Chemists' Society 46(1): 28–30. https://doi.org/10.1007/BF02632705

Atolani O., Adamu N., Oguntoye O.S., Zubair M.F., Fabiyi O.A., Oyegoke R.A., Adeyemi O.S., Areh E.T., Tarigha D.E., Kambizi L. and Olatunji G.A., 2020. Chemical characterization, antioxidant, cytotoxicity, anti-toxoplasma gondii and antimicrobial potentials of the Citrus sinensis seed oil for sustainable cosmeceutical production. Heliyon 6(2): e03399. https://doi.org/10.1016/j.heliyon.2020.e03399

Atolani O., Olabiyi E.T., Issa A.A., Azeez H.T., Onoja E.G., Ibrahim S.O., Zubair M.F., Oguntoye O.S. and Olatunji G.A., 2016. Green synthesis and characterization of natural antiseptic soaps from the oils of underutilized tropical seed. Sustainable Chemistry and Pharmacy 4: 32–39. https://doi.org/10.1016/j.scp.2016.07.006

Bagale R., Acharya S., Gupta A., Chaudhary P., Chaudhary G.P. and Pandey J., 2022. Antibacterial and antioxidant activities of Prinsepiautilis Royle leaf and seed extracts. Journal of Tropical Medicine Article ID 3898939. https://doi.org/10.1155/2022/3898939

Bansal V., Medhi B. and Pandhi P., 2005. Honey—a remedy rediscovered and its therapeutic utility. Kathmandu University Medical Journal 3(3): 305–309.

Bello M.O., Akindele T.L., Adeoye D.O. and Oladimeji A.O., 2011. Physicochemical properties and fatty acids profile of seed oil of Telfairia occidentalis Hook, F. International Journal of Basic and Applied Science11(06): 09–14.

Bhattarai N.K., 1992. Medical ethnobotany in the karnali zone, Nepal. Economic Botany 46(3): 257–261. https://doi.org/10.1007/BF02866624

Chinedu N.U., Benjamin A. and Peter A., 2017. Chemical composition and physicochemical analysis of matured stems of Opuntia dillenii grown in Nigeria. Food Science and Technology 5(5): 106–112. https://doi.org/10.13189/fst.2017.050502

Choi F.D., Juhasz M.L.W., and Mesinkovska N.A., 2019. Topical ketoconazole: a systematic review of current dermatological applications and future developments. Journal of Dermatological Treatment 30(8): 760–771. https://doi.org/10.1080/09546634.2019.1573309

Dhakal B., Thakur J.K., Mahato R.K., Rawat I., Rabin D.C., Chhetri R.R., Shah K.P., Adhikari A. and Pandey J., 2022. Formulation of ebastine fast-disintegrating tablet using coprocessed super disintegrants and evaluation of quality control parameters. Scientific World Journal Article ID 9618344. https://doi.org/10.1155/2022/9618344

Dreno B., Chosidow O., Revuz J., Moyse D., 2003. Study investigator group. Lithium gluconate 8% vs. ketoconazole 2% in the treatment of seborrhoeic dermatitis: a multicentre, randomized study. British Journal of Dermatology 148(6): 1230–1236. https://doi.org/10.1046/j.1365-2133.2003.05328.x

Famurewa J.A., Jaiyeoba K.F., Ogunlade C.A. and Ayeni O.B., 2021. Effect of extraction methods on yield and some quality characteristics of coconut (Cocos nucifera L) oil. Agricultural Engineering International: CIGR Journal. 23(3): 251–260.

Government of India, 2018. Indian pharmacopoeia (IP), vol. 1. Controller of Publications, New Delhi, India, pp. 141–152.

Guan, B., Li, T., Xu, X.K., Zhang, X.F., Wei, P.L., Peng, C.C., Fu, J.J., Zeng, Q., Cheng, X.R., Zhang, S.D. and Yan, S.K., 2014. γ-Hydroxynitrile glucosides from the seeds of Prinsepia utilis. Phytochemistry. 105: 135–140. https://doi.org/10.1016/j.phytochem.2014.05.018

Gultekin F., Yasar S., Gurbuz N. and Ceyhan B.M., 2015. Food additives of public concern for their carcinogenicity. Journal of Nutrition & Food Sciences 3(4): 1–6. https://doi.org/10.15226/jnhfs.2015.00149

Gupta R., Goyal R., Bhattacharya S. and Dhar K.L., 2015. Antioxidative in vitro and antiosteoporotic activities of Prinsepia utilis Royle in female rats. European Journal of Integrative Medicine 7(2): 157–163. https://doi.org/10.1016/j.eujim.2014.10.002

Inekwe U.V., Odey M.O., Gauje B., Dakare A.M., Ugwumma C.D. and Adegbe E.S., 2012. Fatty acid composition and physicochemical properties of Jatropha Curcas oils from Edo and Kaduna states of Nigeria and India. Annals of Biological Research 3(10): 4860–4864.

Islam, M.R., Beg, M.D.H. and Jamari, S.S., 2014. Alkyd based resin from non-drying oil. Procedia Engineering 90: 78–88. https://doi.org/10.1016/j.proeng.2014.11.818

Jagdale S., Bhavsar D., Gattani M., Chaudhari K. and Chabukswar A., 2011. Formulation and evaluation of miconazole nitrate soap strips for dermal infections. International Journal of Pharmacy and Pharmaceutical Sciences 3(3): 299–302.

Kewlani P., Tiwari D.C., Singh B., Negi V.S., Bhatt I.D. and Pande V., 2022a. Source-dependent variation in phenolic compounds and antioxidant activities of Prinsepia utilis Royle fruits. Environmental Monitoring and Assessment 194(3): 1–5. https://doi.org/10.1007/s10661-022-09786-z

Kewlani P., Tewari D.C., Singh L., Negi V.S., Bhatt I.D., Pande V., 2022b. Saturated and polyunsaturated fatty acids rich populations of Prinsepia utilis Royle in western Himalaya. Journal of Oleo Science 71(4): 481–491. https://doi.org/10.5650/jos.ess21262

Kim S.A., Moon H., Lee K. and Rhee M.S., 2015. Bactericidal effects of triclosan in soap both in vitro and in vivo. Journal of Antimicrobial Chemotherapy 70(12): 3345–3352. https://doi.org/10.1093/jac/dkv275

Koirala S., Nepal P., Ghimire G., Basnet R., Rawat I., Dahal A., Pandey J. and Parajuli-Baral K., 2021. Formulation and evaluation of mucoadhesive buccal tablets of aceclofenac. Heliyon 17(3): e06439. https://doi.org/10.1016/j.heliyon.2021.e06439

Krist S., 2020. Vegetable fats and oils. Springer Nature, New York, NY. https://doi.org/10.1007/978-3-030-30314-3

Kunwar R.M. and Duwadi N.P.S., 2003. Ethnobotanical notes on flora of Khaptad National Park (KNP), far-western Nepal. Himalayan Journal of Sciences 1(1): 25–30. https://doi.org/10.3126/hjs.v1i1.182

Maikhuri R.K., Singh A. and Semwal R.L., 1994. Prinsepia utilis Royle: a wild, edible oil shrub of the higher Himalayas. Plant Genetic Resources Newsletter 98: 5–8.

EthnopharmacologyManandhar N.P., 1986. Ethnobotany of jumla district, Nepal. Pharmaceutical Biology 24(2): 81–89. https://doi.org/10.3109/13880208609083311

Manandhar N.P., 1995. A survey of medicinal plants of Jajarkot district, Nepal. Journal of Ethnopharmacology 48(1): 1–6. https://doi.org/10.1016/0378-8741(95)01269-J

Mekkawy A.I.A.A., Fathy M. and El-Shanawany S., 2013. Study of fluconazole release from O/W cream and water soluble ointment bases. British Journal of Pharmaceutical Research (4): 686–696. https://doi.org/10.9734/BJPR/2013/3702

Muhammad A., Ayub M., Zeb A., Wahab S. and Khan S., 2013. Physicochemical analysis and fatty acid composition of oil extracted from olive fruit. Food Science and Quality Management 19(1): 1–6.

Mwanza C. and Zombe K., 2020. Comparative evaluation of some physicochemical properties on selected commercially available soaps on the Zambian market. Open Access Library Journal 7(3): 1–3. https://doi.org/10.4236/oalib.1106147

Naveed S. and Jaweed L., 2014. UV spectrophotometric assay of ketoconazole oral formulations. American Journal of Life Sciences 2(5): 108–111.

Nierat T.H., Musameh S.M. and Abdel-Raziq I.R., 2014. Temperature-dependence of olive oil viscosity. Materials Science 11(7): 233–238.

Nowak K., Ratajczak–Wrona W., Górska M. and Jabłońska E., 2018. Parabens and their effects on the endocrine system. Molecular and Cellular Endocrinology 474: 238–251. https://doi.org/10.1016/j.mce.2018.03.014

Oladiji A.T., Yakubu M.T., Idoko A.S., Adeyemi O. and Salawu M.O., 2010. Studies on the physicochemical properties and fatty acid composition of the oil from ripe plantain peel (Musa paradisiaca). African Scientist 11(1): 73–78.

Pandey J., Bastola T., Tripathi J., Tripathi M., Rokaya R.K., Dhakal B., Bhandari R. and Poudel A., 2020. Estimation of total quercetin and rutin content in Malus domestica of Nepalese origin by HPLC method and determination of their antioxidative activity. Journal of Food Quality. 2020:1-13. https://doi.org/10.1155/2020/8853426

Pandey J., Khanal B., Bhandari J., Bashyal R., Pandey A., Mikrani A.A., Aryal P. and Bhandari R., 2021. Physiochemical evaluation of Diploknema butyracea seed extract and formulation of ketoconazole ointment by using the fat as a base. Journal of Food Quality. 2022:1-11. https://doi.org/10.1155/2021/6612135

Rane S.S. and Padmaja P., 2012. Spectrophotometric method for the determination of ketoconazole based on amplification reactions. Journal of Pharmaceutical Analysis 2(1): 43–47. https://doi.org/10.1016/j.jpha.2011.10.004

Ruckmani K., Krishnamoorthy R., Samuel S., Linda H. and Kumari J., 2014. Formulation of herbal bath soap from Vitex negundo leaf extract. Journal of Chemical and Pharmaceutical Sciences 2(2): 95–99.

Samuel C.B., Barine K.K. and Joy E.E., 2017. Physicochemical properties and fatty acid profile of shea butter and fluted pumpkin seed oil, a suitable blend in bakery fat production. International Journal of Nutrition and Food Science 6(3): 122–128. https://doi.org/10.11648/j.ijnfs.20170603.12

Sharma K.P., Belbase A. and Neupane U., 2020. Quality control and evaluation of certain properties of soaps available in Butwal sub-metropolitan city, Nepal. Butwal Campus Journal 2(1): 6–12. https://doi.org/10.3126/bcj.v2i1.35664

Shirsand S.B., Para M.S., Nagendrakumar D., Kanani K.M. and Keerthy D., 2012. Formulation and evaluation of ketoconazole niosomal gel drug delivery system. International Journal of Pharmaceutical Investigation 2(4): 201–208. https://doi.org/10.4103/2230-973X.107002

Sindhu R.K., Chitkara M., Kaur G., Kaur A., Arora S. and Sandhu I.S., 2019. Formulation development and antimicrobial evaluation of polyherbal soap. Plant Archives 19: 1342–1346.

Staub I., Flores L., Gosmann G., Pohlmann A., Froeehlich P.E., Schapoval E.E. and Bergold A.M., 2010. Photostability studies of ketoconazole: isolation and structural elucidation of the main photodegradation products. Latin American Journal of Pharmacy 29(7): 1100–1106.

Tareau M.A., Palisse M. and Odonne G., 2017. As vivid as a weed… Medicinal and cosmetic plant uses amongst the urban youth in French Guiana. Journal of Ethnopharmacology 203: 200–213. https://doi.org/10.1016/j.jep.2017.03.031

Teixeira C.B., Macedo G.A., Macedo J.A., da Silva L.H. and Rodrigues A.M., 2013. Simultaneous extraction of oil and antioxidant compounds from oil palm fruit (Elaeisguineensis) by an aqueous enzymatic process. Bioresource Technology 129: 575–581. https://doi.org/10.1016/j.biortech.2012.11.057

Touré A., Bahi C., Bagré I., N'guessan J.D., Djama A.J. and Coulibaly A., 2010. In vitro antifungal activity of the soap

formulation of the hexane leaf extract of Morindamorindoides (Morinda; Rubiaceae). Tropical Journal of Pharmaceutical Research 9(3): 237–241. https://doi.org/10.4314/tjpr.v9i3.56283

Udensi E.A. and Iroegbu F.C., 2007. Quality assessment of palm oil sold in major markets in Abia state, Nigeria. Agro-Science 6(2): 25–27. https://doi.org/10.4314/as.v6i2.1566

Watanabe T., Rajbhandari K.R., Malla K.J., Devkota H.P. and Yahara S., 2013. Medicinal plants of Nepal. Ayurseed Life Environmental Institute, Kanagawa, Japan, 381 p.

Widyaningsih S., Chasani M. and Diastuti H., 2018. Novayanti. Formulation of antibacterial liquid soap from nyamplung seed oil (Calophyllum inophyllum L) with addition of Curcuma heyneana and its activity test on Staphylococcus aureus. IOP Conference Series: Materials Science and Engineering (MSE) 349: 1–9. https://doi.org/10.1088/1757-899X/349/1/012062

Winnicka K., Wroblewska M., Wieczorek P., Sacha P.T. and Tryniszewska E., 2012. Hydrogel of ketoconazole and PAMAM dendrimers: formulation and antifungal activity. Molecules 17(4): 4612–4624. https://doi.org/10.3390/molecules17044612

Yadav S., 2018. Edible oil adulterations: current issues, detection techniques and health hazards. International Journal of Chemical Studies 6(2): 1393–1397.

Yang J., Yang Z.w., Yi P., Huang D.s. and Min Y., 2012. Fatty acid compositions in seeds of Prinsepia utilis Royle. Journal of Honghe University. p. 4.

Yermanos D.M., Hemstreet S., Saleeb W., Huszar C.K., 1972. Oil content and composition of the seed in the world collection of sesame introductions. Journal of the American Oil Chemists' Society (1): 20–23. https://doi.org/10.1007/BF02545131

Yu J.J., Manus M.B., Mueller O., Windsor S.C., Horvath J.E. and Nunn C.L., 2018. Antibacterial soap use impacts skin microbial communities in rural Madagascar. PloS One 13(8): e0199899. https://doi.org/10.1371/journal.pone.0199899

Zhang X., Jia Y., Ma Y., Cheng G. and Cai S., 2018. Phenolic composition, antioxidant properties, and inhibition toward digestive enzymes with molecular docking analysis of different fractions from Prinsepia utilis Royle fruits. Molecules 23: 3373. https://doi.org/10.3390/molecules23123373

Zheng Y., Zhao L. and Yi J., 2022. Phytochemical characterization and antioxidant and enzyme inhibitory activities of different parts of Prinsepia utilis Royle. Journal of Food Quality. Article ID 9739851. https://doi.org/10.1155/2022/9739851