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Preparation and Evaluation of Voriconazole as Topical Organogel

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Abstract

Voriconazole is a triazole antifungal drug that inhibits fungal ergosterol synthesis. It is used to treat invasive fungal infections of a wide range of fungal species. Organogel is a semisolid preparation in which the apolar phase becomes immobilized within the three-dimensional structure. It would be good to have a topically applied form of voriconazole organogel to avoid undesirable systemic side effects and to reduce the dosage by coming into direct contact with the pathological site. This study aimed to formulate topical voriconazole organogel, consisting of a low molecular weight gelator (palmitic acid) at different concentrations with oleic acid, grape seed, and sesame oil. A solubility study revealed that voriconazole was highly soluble in the chosen oils. Several gelator concentrations were prepared by dissolving the drug in the oil at 85 °C, adding the gelator while continuously stirring for 40 minutes to obtain a clear solution, then allowing the mixture to cool to room temperature (24±2°C) to solidify. Formulas were prepared and evaluated based on their physical appearance, transition temperature, spreadability, viscosity, pH, *in-vitro* drug release study, antifungal study, Transmission electron microscopy (TEM), and skin irritation test with histological examination. A compatibility study was conducted using Fourier-transform infrared (FT-IR) spectral analysis; it showed that the drug and excipients did not significantly interact. All the designed formulations of voriconazole showed acceptable physical properties, suitable pH for the skin, acceptable gel-solution, and solution-gel transition temperature. The viscosity study demonstrated the pseudo-plastic shear thinning behavior of the organogels. Among all formulations, palmitic acid with grape-seed oil at its minimum gelation concentration (MGC) showed better drug release for sustained topical drug delivery; from the above observation results that this palmitic acid with grape-seed oil formulation might be a more promising topical treatment option for the recovery of skin fungal infections.

Keywords: Voriconazole, Palmitic acid, Organogel, Grape-seed oil, Gelator.

Introduction

Topical medication administration is an effective method of treating both local and systemic disorders [(1)]. Topical medications are considered a helpful treatment option for certain localized dermatological disorders when other routes are unfavorable mostly due to GIT side effect. It may also penetrate through the skin's underlying layers, enabling higher absorption and, consequently, the intended pharmacological systemic impact [(2, 3)]. Among other pharmaceutical dosage forms for topical medication delivery include sprays, solid powders, liquid formulations, and semisolids. Gels, creams, and ointments are the most popular semisolid drug delivery formulations for topical application [(4)]. Gels have superior application properties and stability compared to other semisolid preparations [(5)]. Targeting the infection site, lowering the possibility of systemic side effects, increasing treatment efficacy, and promoting high patient compliance are among the numerous advantages of topical treatment for fungal infections [(6)].

Various dermatological skin infections have been treated with several topical effective antifungal agents [(7)]. A gel is defined as a semi-solid formulation having an tendency to immobilize the internal solvent phase within the three-dimensional networked structure spaces, which is either non-polar solvent (organogel), or polar solvent (hydrogel) [(8)]. Organogels are gels made of non-aqueous liquids that are not crystalline or glassy and comprise a liquid organic phase entangled in a three-dimensional network [(9)]. It could maintain thermodynamic stability due to the prompt development of fibrous structures. It performs efficiently for topical medication delivery of lipophilic compounds [(10)]. Through percutaneous

immunocompromised patients; examples include invasive mycoses, emerging fungal infections, and invasive candidiasis [12]. VRC has an enhanced affinity for 14-alpha sterol demethylase, making it useful in treating fungal infections that have grown resistant to fluconazole [13]. VRC is a class II drug, which means it has good permeation but poor water solubility [14]. This work aimed to develop an organogel formulation of VRC using palmitic acid (PA) as a gelling agent. Oleic acid oil (OO), grapeseed oil (GO), and sesame oil (SO) as organic solvents, the influence of the gelling agent type and concentration, and the solubility of the drug in different oils were investigated. The characterization of the drug, minimum gelation concentration MGC, physical appearance, pH measurement, spread-ability, Transition temperature, oil binding capacity (OBC), in-vitro drug release, antifungal activity, Transmission electron microscopy (TEM) and skin irritation test with histological examination were evaluated. The objective of the present study is to develop a novel topical VRC organogel for sustained delivery of the drug, ease application, decrease the drug side effect, improved availability at the desired site, and improved patient compliance.

Materials and Methods

Materials

Voriconazole was a kind gift from Sama Alfayhaa for the pharmaceutical industry/Iraq, palmitic acid was purchased from Alpha Chemika/India, oleic acid oil, grape-seed oil, and sesame oil were purchased from Loba Chemie /India, Stilla classic/Spain and Iko /India respectively.

Saturated solubility of VRC

Using a vortex mixer, an excess of VRC was added to 3 mL of chosen oils in 10 mL capacity stopper vials to assess the solubility of VRC in the different oils (OO, GO, and SO) and in phosphate citrate buffer pH 5.5. Then, in a water bath shaker, the mixture vials were shaken for 72 hours at 24 ±0.5°C. A 0.45 μm membrane filter was then used to filter the oils and buffer (to remove non dissolved drug). after that the filtrates of oils had been diluted with methanol [15] and the VRC in buffe r filtrate diluted with buffer, the VRC concentration was subsequently measured using a UV spectrophotometer at λ max 256 nm using the calibration curve equation of VRC in methanol (y=0.0239x+0.0113) with R2=0.9996 and in buffer (y=0.0214x+0.0068) with R2=0.9991

Preparation of organogel and minimum gelation concentration MGC

To determine the MGC of PA in each oil, the blank organogel was first prepared. This was accomplished by weighing the specific weight of PA (to get the desired concentration) in the vials and then completed to 1 g with OO, GO, and SO at the following concentrations: (15,17,20,22,25,27,30,32) wt.% for OO, and (2,4,6,8,10,12,14,16) wt.% for GO and SO. To verify that PA was soluble in oils, the vials were incubated in the water bath, and stirred for 30 minutes at 85°C, the vials were left to cool to room temperature (24 ±2°C). After a while, the vials were turned upside down to verify the minimum gelation concentration of the organogel composition. When there is no flow, a solid organogel is produced; nevertheless, if flow happens during overturning, a liquid organogel is produced [16]. The concentrations of PA that produced solid organogel were selected for incorporation of the VRC. After solubilizing 1% w/w of the VRC with the selected amount of oil then the gelator was added and stirred for 40 minutes at 85 ºC [17].

Organoleptic characteristics

Color, texture, phase separation, homogeneity and grittiness were assessed [9].

Transition temperature

The vials containing the VRC organogels were heated to 24 °C in a water bath. After that, the temperature increased by 2°C every 15 minutes to a maximum of 85°C. The vials were inverted every fifteen minutes to observe the organogel formulation's flow. This is known as the gel-sol point (T gel-sol), which is reached when the organogel begins to flow. After that, the vials went through another phase; the temperature was lowered by 2°C every 15 minutes until it reached 24 °C to record the gelation points (T sol-gel) [18].

Oil binding capacity (OBC)

Since the strength of the scaffold that builds an organogel and holds the oil is reflected in the organogels binding capacity (19). We measure the OBC of prepared organogels. One gram of VRC organogel was centrifuged at 6000 rpm for fifteen minutes in a vial; the vials were turned upside down and placed on top of the filter paper for five minutes, allowing the free oil to fall from the organogels to be collected. The filter paper was then weighed to determine the amount of oil eliminated. To calculate OBC (%), use equation 1 [20].

$$\%OBC = \left(1 - \frac{mass\ of\ unbound\ oil}{initial\ sample\ mass}\right) \times 100 \quad \text{.....Eq1....}$$ [21].

Determination of pH

Digital pH meter (Hanna instruments, USA) was used to record the pH of each VRC organogel. After 24 hours of formulation, organogels were immersed in electrode without dilution, and pH meter measurements were recorded [22, 23].

Determination of Spreadability

To test the spreadability of prepared organogel, 0.5 g of the prepared VRC organogel was placed on a 2.5 * 7.5 cm glass the slide in a previously marked circle with a diameter of 1 cm [15]. A second glass slide of the same size was then placed over the first, sandwiching the gel between the upper and lower slides. The organogel between the two slides was subjected to compression by a five-gram weight placed on the upper slide for five minutes. The resulting change in diameter of the gel's spread was measured [21, 24].

Viscosity studies

A viscosity analysis was carried out using a (rotary viscometer VR3000, Myr, Spain). Samples were sheared with spindle number R6 at 5, 10, 30, 50, 100, and 200 rpm up and down (We use R6 spindle according to the try and error method. To obtain valid measurement, the torque value must be between 10 % and 100 %. If the torque value is higher than 100 %, you need to use a smaller spindle. If the torque value is lower than 10 %, you need to use a bigger spindle). Prior to reading, each sample was sheared for thirty seconds. Plots of shear stress (rpm) against viscosity (mPa.s) were used to analyze rheological behavior [25, 26].

FTIR Analysis

Fourier-transform infrared spectroscopy (Model: Alpha-e; Bruker, Germany) was used to investigate the FTIR spectra of organogel formulations. The formulations' spectra were obtained in the wavenumber range of 4000–600 cm−1 using attenuated total reflection mode [27]. The result was analyzed using origin lab software 24.

In- vitro release study

A thin layer of one gram of organogels, equivalent to 10 mg of VRC, was applied to the watch glass's surface with a 7 cm diameter. The sample was covered with a stainless-steel screen with 150 pores per inch [28]. The assembly is positioned at the bottom of a 500 mL jar with citrate phosphate buffer saline pH 5.5 as a dissolution medium [22, 29] (according to the compatibility with skin pH) (30, 31), at 34 °C±0.5 in USP dissolution test apparatus type II, in which paddle was rotated at 75 rpm (32). A control of 1% of VRC in each oil was run with the release studies of organogels to be compared with the organogels The control was prepared as a fact of the ability oil to hinder the hydrophobic drugs release [21, 33]. At 1, 2, 3, 4, 5, 6, 7, and 8 hours, five mL samples were taken out of the jar, and the withdrawn samples were refilled with the same volume of new buffer solution to maintain the sink condition. The samples were filtered using a 0.45 μm filter syringe and analyzed using spectrophotometric analysis for VRC at its λmax of 256 nm [28].

Antifungal sensitivity test

Broth micro and macro-dilution is one of the most basic anti-microbial susceptibility testing methods. In this study, we used the macro dilution test. Two pure isolation strains of candida albicans were prepared as a fungal suspension (The standard strain of Candida albicans was cultivated on Sabouraud dextrose agar medium and incubated at 37°C for 48 hours. Following this, some fungal colonies were dissolved in distilled water until the suspension's stiffness changed to equal 0.5 MC Farland, indicating that 1.5 × 108 microbial cells are present in 1 ml of the microbial suspension). Mix an equal amount (2 mL) of fungal suspension, the selected formula, and the blank organogel (without VRC) separately, and put the mixture in the incubator for 15 minute [34]. Then, 100 μL from the mixture above were transferred to a tube containing the sterilized nutrient liquid medium; the inoculated tubes were incubated for 24hr without agitation (agitation lead to dissolve oxygen in medium and increase the fungal growth [35]. The result will be shown in this test by noticing the presence of fungal growth in the case of affectivity or no affectivity of the formula on the fungus [34, 36].

Transmission electron microscopy (TEM)

The organogel microstructure was ascertained using morphological analysis and transmission electron microscopy (TEM). A single drop (10μL) of the sample was placed on a copper grid coated with carbon and left to dry for 60 seconds. Subsequently, a drop of 2% uranyl acetate solution was applied to the grids for 50 seconds, and any remaining stain was removed using filter paper. Using a TEM (Jeol JEM-2100, Jeol Ltd., Tokyo, Japan) with an acceleration voltage of 120 kV, the air-dried materials were examined [37] .

Skin Irritation Studies

In this model investigation, skin irritation was assessed in healthy male Wister Albino rats weighing 250–350 g and two to three months old. The hairs on each rat's abdomen were shaved [38]. The examined area was rubbed with dry cotton, and then the formula was applied. Three groups (gp), each with two rats, were used to conduct the Draize patch test in order to examine skin sensitivity. The groups were as follows:gp 1: treated with the chosen formula; gp 2: treated with a common irritant, a 0.8% v/v formalin water solution. gp3: left without treatment [39].

Histological examination

After euthanizing the rats they underwent the irritancy test, the examined skin was cuted into pieces and dyed. The skin was colored and sliced into pieces. Subsequently, sections of rat skin were placed within paraffin wax blocks and sliced into 5-mm-long pieces using an electrical microtome. In order to examine under a microscope, these samples were sliced and stained with hematoxylin and eosin (H&E) dyes [40].

Statistical analysis

Measurements were carried out in triplicates and subjected to statistical analysis, with the mean value

followed by the standard deviation (± SD) [41]. One-way ANOVA was performed using SPSS version 21. The similarity test f2 was utilized for the in-vitro release.

Results and Discussion

Saturated solubility of VRC

As shown in Figure 1, the solubility was 33.66±1.102, 30.33±1.155, 27.66±1.443and 0.861±0.73 mg/mL in OO, GO, SO, and citrate phosphate buffer 5.5, respectively. Oils were selected based on their higher solubilizing capacity for the VRC drug, so they are used in this study.

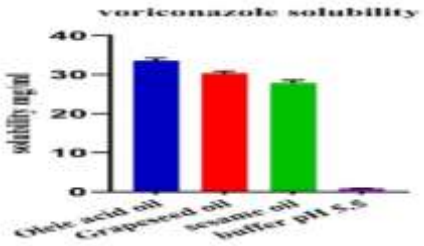

Figure 1. Solubility of voriconazole in oils and citrate phosphate buffer (pH 5.5).

Formulation of organogel

Quantitative assessment of the organogel establishes the gelation ability by determining the MGC. The MGC of PA in oil was determined using organogel formulations that remained solid and did not flow when the vials were turned upside down at room temperature. Figure 2 shows that the MGC of PA was 17wt%, 8wt%, and 4wt% in OO, GO, and SO, respectively. The differences in the MGC can be related to the different solubility of PA in oils. Subsequently, the VRC was added into three organogels, starting with the lowest concentration of PA those oils had gelled as shown in Table 1. The gelation time of all prepared organogel was about 15-30 minute.

Table 1. The organogel names composition as 1% (w/w) VRC in each organogel.

Formulation Name *	PA %(w/w)	Oil Up to 1g
17POO	17	OO
20POO	20	OO
22POO	22	OO
8PGO	8	GO
10PGO	10	GO
12PGO	12	GO
4PSO	4	SO
6PSO	6	SO
8PSO	8	SO

* P (palmitic acid), OO (oleic acid oil), GO (grapeseed oil), SO (sesame oil).

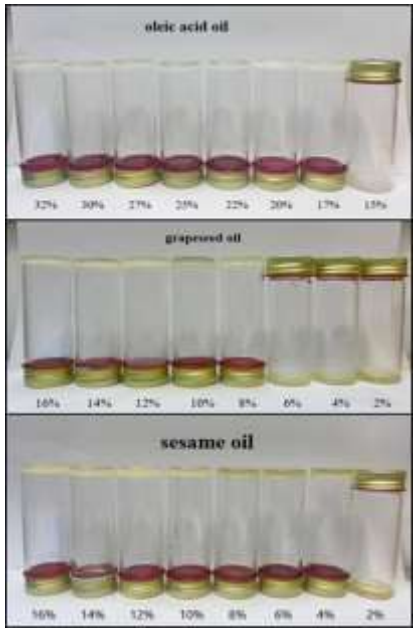

Figure 2. Organogels of PA in oleic acid, grape-seed, and sesame oil (without drug) as the inverted vials are referred to as solid.

Organoleptic characteristics

The generated organogels exhibited a smooth texture, non-transparent, and demonstrated good homogeneity without grittiness or phase separation.

Transition temperature

As increasing the temperature of the organogels, there was a corresponding surface free energy increase, with an increase in the mobility of gelator molecules constituting the 3D-self-assembled structure of the organogel formulations. The breakdown of the networked structure resulted from further temperature increases, which completely disrupted the interaction between self-assembled structures. This allowed the gelled system to acquire a sol state and flow freely, which is why an increase in organogel concentration raises the temperature required for the organogels to flow [(42)]. The temperatures at which the phase changes from gel to sol and vice versa are listed in Table 2. The VRC organogels changed from solid to liquid at temperatures well above the normal body temperature; thus it will remain in semisolid consistency throughout the application (unless the patient have a very high fever). These results agree with previous study [(43)]. However, the decrease in temperature lead to slow down of molecular interactions, leading to the organogel back again to its initial structure. The organogels' thermo-reversibility characteristic accounts for this entire behavior [(44)]. ANOVA test showed that there is a significant difference between the formulas ($p<0.05$).

Oil binding capacity (OBC)

As shown in Table 2, a significant correlation existed between the concentration of organogels and the OBC, suggesting that the concentrated organogels effectively comprised the solvents. This is comparable to the pattern of increasing folic acid concentration in organogel [(45)]. Using the ANOVA test to perform statistical analysis showed that the variation in OBC amongst the organogel was significant ($p < 0.05$).

Determination of pH

As seen in Table 2, the pH levels of VRC organogels ranged from 5.56 to 6.22; since the pH range of the organogel (4–6) was compatible with the almost acidic pH of the skin, there was no risk of skin irritation. These findings were agreed with the azithromycin grapeseed oil organogels [(46)].

Determination of Spreadability

This test showed the ability of skin preparation to spread evenly across the skin when applied topically. Our findings, as seen in Table 2, showed that the most readily spread organogel was 8PGO, and this capacity decreased as the concentration of the PA increased; this may be due to the strong network that preventing the molecules from spreading more readily and the lower surface tension of the least concentration organogel [(47)].Statistically there is a significant difference between the spreadability result of prepared formulas ($p<0.05$).

Table 2. Shows the tabulated results presenting the T sol-gel, T gel-sol, OBC%, pH, and spreadability results for VRC organogel.

Organogel	(T sol-gel) °C±SD	(T gel-sol) °C±SD	OBC %±SD	pH ±SD	Spreadability in cm ±SD
17POO	31.33±0.57	37.00±0.64	88.55±0.83	5.80±0.10	2.26±0.05
20POO	30.33±0.64	38.66±0.75	92 .55 ± 0.83	5.70±0.12	2.01±0.10
22POO	30.11±0.68	41.33±0.57	100.22±0.82	5.56±0.05	1.87±0.05
8PGO	32.33±0.54	40.66±0.75	91.55±0.1.15	6.13±0.06	2.91±0.22
10PGO	31.44±0.73	40.66±0.57	92.33±0.81	5.91±0.12	2.82±0.12
12PGO	31.11±0.68	42.66±0.61	95.55±0.81	5.70±0.21	2.61±0.21
4PSO	30.33±0.57	38.33±0.68	75.22±1.15	6.22±0.21	2.62±0.10
6PSO	30.44±0.68	39.33±0.57	83.22±0.82	6.21±0.10	2.31±0.05
8PSO	29.44±0.57	41.66±1.15	85.22±-0.57	6.12±0.12	1.91±0.10

Viscosity study

The viscosity study of the organogel formulations exhibited the non-Newtonian shear thinning pseudoplastic type of flow, i.e., decreases in viscosity at increasing shear rates. As the shear stress increases, the gelling material's disordered molecules are forced to align their long axes with the flow direction. This orientation lowers the material's viscosity and internal resistance [(22)]. At the same time, the result showed that the viscosity of the prepared VRC organogel was increases as the concentration of PA increases in each oil, as seen in Figure 3.

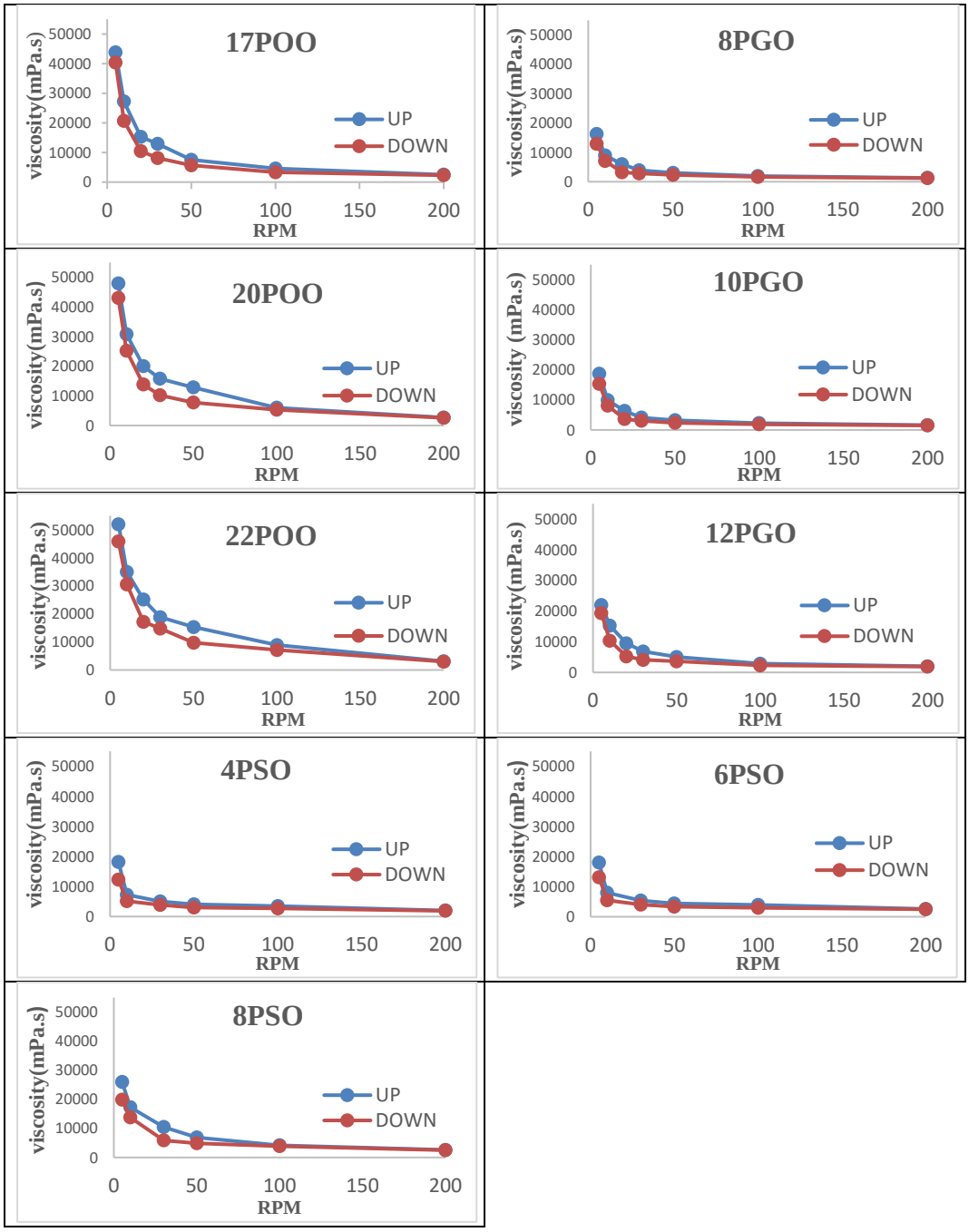

Figure 3. Viscosity of VRC organogel formulations.

FTIR analysis

FTIR spectra study gives information about functional groups and molecular interactions within the different components of the formulations. In our study, the FTIR analysis of the lowest gelator concentration formula of each oil used in this study has been shown in Figure 4. All organogel formulations showed peak in the 3700–3200 cm−1 range. The intensity of the peak may be explained by the presence of a stretching O─H hydrogen bond [48]. The hydrogen bonding likely had a significant effect on the creation of the gelator network while the gelation process occurred [49]. The medicated formulations contain only 1% VRC and 99% rest of the excipients so many peaks are merged in FTIR spectra [9]. As seen in Figure 4, pure VRC peak showed the –OH stretching peak at around 3189.9 cm−1, C–N peak at around 1128.5 cm−1, and C–F peak at 1403.89 cm−1. The Formulas showed a characteristic peak at 1707 cm−1, 1741 cm−1, and 1743 cm−1 for the formula POO, PGO, PSO respectively, which is the peak of the carbonyl gp that found in oil of that formula. The dual peak at ≈ 2920 cm−1 and ≈ 2850 cm−1 can be explained due to C-H stretching vibration from the CH3 and CH2 groups, which are present in both oils and PA [50]. No additional peak indicated no irreversible interactions between VRC and excipients [27].

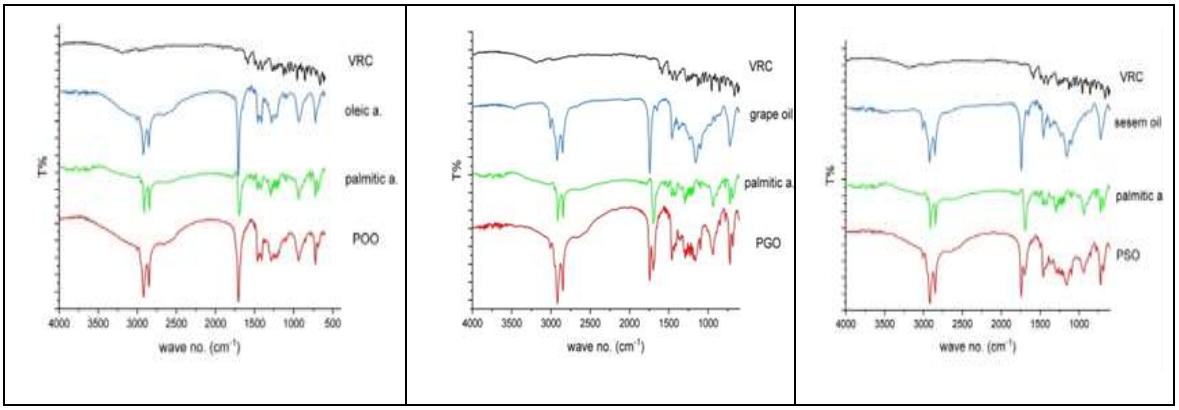

Figure 4. FTIR of VRC drug and organogel formulas.

In-vitro release study

An *in-vitro* release study was conducted using VRC organogels for 8 hours. As shown in Figure 5, since varied concentrations of PA were utilized as a gel matrix, the structure of gelators and organic fluids significantly impacted the controllable release and release ratios of VRC. As a result, the release profiles of VRC demonstrate a sustained release behavior. The release ratios of VRC after 8 hr in citrate phosphate buffer saline (pH 5.5) found to be 74%,67%,60% for 17POO,20POO and 22POO respectively and 100%,92%,82% for 8PGO,10PGO,12 PGO respectively and, 86%,75%,72 %for 4PSO,6PSO and 8PSO respectively. In the present study, as the concentration of the organogel increases, it decreases the drug's release percentage; this result and the low release rates of drug molecules can be attributed to the presence of dense 3D networks formed by increasing concentrations of PA[51]. In other words, the diffusion of VRC must overcome more obstacles and use more zig-zag pathways within the organogel. This result agrees with the result of cinnarizine organogel [18]. The control of VRC in OO, GO, and SO showed non-similar with the similarity factor (f2 <50) in the VRC release profile to the organogels. From the results of the spreadability test, the VRC organogels with lower gelator concentrations exhibited greater spreadability. The in vitro release study demonstrated a consistent pattern where the organogels with the
lowest concentration of PA in different solvents exhibited a higher release of VRC. Both outcomes contributed to achieving the objective of this study to increase VRC availability through the skin; hence, the 8PGO organogels were processed for further studies

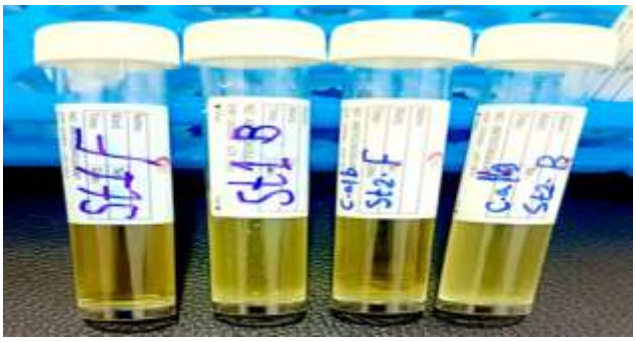

Figure 5. The in-vitro release profile of organogel, a: oleic acid oil formulas b: grape-seed oil formulas c: sesame oil formulas, using palmitic acid as a gelator, in citrate phosphate buffer saline (pH 5.5).

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Antifungal sensitivity test

As shown in Figure 6, there is no growth in tubes treated with a mixture of the fungus and the 8PGO formula, (clear appearance) and the turbid appearance of fungus growth in the tube results from the treatment of blank organogel with the fungi.

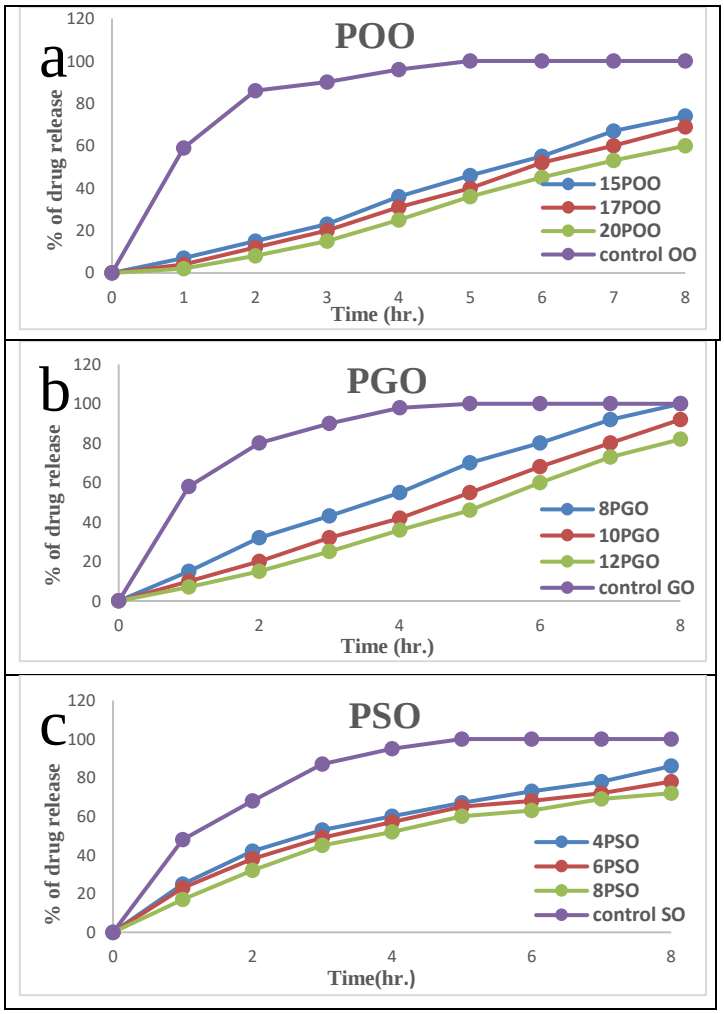

Figure 6. The antifungal activity of VRC in two pure strains of candida albicans for F (8PGO) formula and B blank organogel (without VRC).

Transmission electron microscopy (TEM)

TEM is an analytical technique used to visualize the smallest structures in matter. The image of optimized formulation (8PGO) was observed using TEM, as shown in Figure 7. TEM shape analysis of the organogel showed nano to micro-scale structures. The shape of droplets was found to be spherical. This spherical shape is due to fatty acid vesicles formation from hydrocarbon single-chain surfactants [51] which is PA in our study. Most of the droplets were of approximately uniform size and shape. Same spherical shape were shown for pure palmitic acid TEM [52]. Same trend of image was showed with fish oil beeswax oleogel [53].

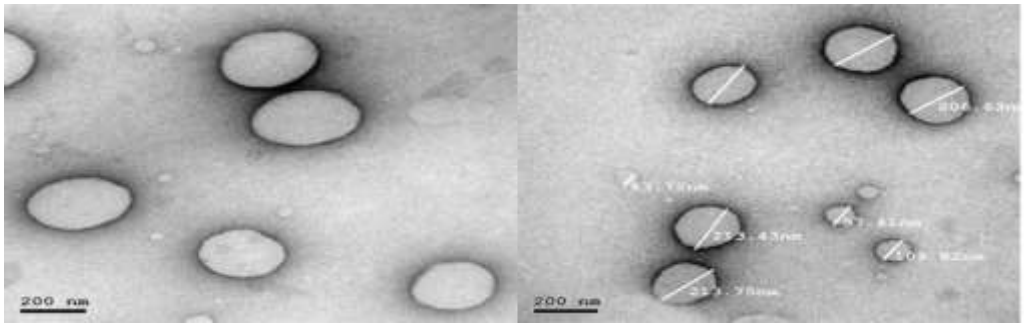

Figure 7. TEM (Transmission Electron Microscope) image of formula 8PGO inserts: size measurements of the micelle.

Skin irritation studies

To assess the degree of skin irritation, a visual scoring system was employed:"0" indicated the absence of skin discomfort. "1" indicated minor skin irritation, "2" indicated clear skin irritation, "3" indicated moderate skin irritation, and "4" indicated scarring on the skin [39]. The 8PGO formula resulted in a skin irritation observation score of 0. On the

other hand, the formalin score was 4, suggesting that the organogels were not irritating when compared to formalin, which caused significant redness and edema [21].

Histological examination

The skin from the irritancy test was studied histologically,skin for control and treated with 8PGO formula showed normal view of epidermis EP (keratinocytes KC and stratified squamous epithelial cells SC), dermis DR (collagen fibers CF, fibrocyes/blasts FC), hair follicles HF, sebaceous glands SB , hypodermis layers (adipose cells AC) [54]. However skin treated with formalin showing continuous epidermis, flattened dermoepidermal junction, and marked epithelial shedding, a very thin epidermis, degenerated fibrous tissue. To conclude, the 8PGO histological image revealed no changes on the normal composition of the skin upon application of 8PGO. That can be shown in Figure 8.

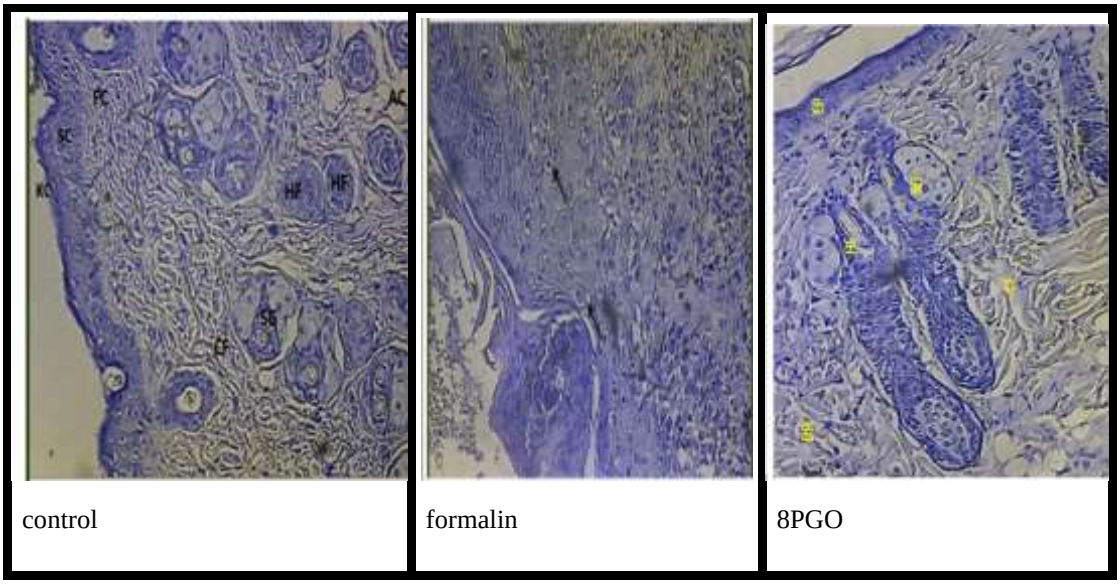

Figure8 . Microscopic images histopathology study for VRC organogel, at a magnification of 100x. The inset in forrmalin slide shows epidermal cells with vacuolated cytoplasm (→).

Conclusion

Based on the results, we concluded that palmitic acid gave good gelation to oils OO, GO, and SO. Indeed, the organogels 8PGO, amongst other investigated organogels, achieved the highest percent of release with good spreadability, oil binding capacity, and *in-vitro* antifungal activity, no skin irritation; hence, this organogel was a good candidate for voriconazole as sustained release topical formulation.

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Conflicts of Interest

No competing interests were disclosed.

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Ethics Statements

This research was approved by University of Baghdad-Collage of Pharmacy Research Ethics Committee, Baghdad, Iraq, ethical approval number RECAUBCP132024G.

Author Contribution

Study conception and design: Hiba Muneer Fysal, Hanan Jalal Kassab; data collection: Hiba Muneer Fysal; analysis and interpretation of results: Hiba Muneer Fysal, Hanan Jalal Kassab; draft manuscript preparation: Hiba Muneer Fysal, Hanan Jalal Kassab. All authors reviewed the results and approved the final version of the manuscript.

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تحضير وتقييم للفوريكونازول كهلام عضوي موضعي

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الخلاصة

يثبط دواء تريازول المضاد للفطريات، فوريكونازول، تخليق الإرغوستيرول الفطري ويتفاعل بشكل جيد للغاية ضد مجموعة واسعة من الأنواع الفطرية. الهلام العضوي هو مستحضر شبه صلب حيث يصبح الطور القطبي غير متحرك داخل البنية ثلاثية الأبعاد. سيكون من الجيد أن يكون لديك شكل موضعي من دواء الفوريكونازول لتجنب الآثار الجانبية الجهازية غير المرغوب فيها ولتقليل الجرعة عن طريق الاتصال المباشر بالموقع المرضي. تهدف هذه الدراسة إلى تركيب جل عضوي فوريكونازول موضعي يتكون من معامل الهلام منخفض الوزن الجزيئي (palmitic acid) بتركيزات مختلفة مع زيت بذر النخيل وزيت بذور العنب وزيت السمسم. كشفت دراسة الذوبان أن دواء الفوريكونازول قابل للذوبان بدرجة جيدة في الزيوت المختارة. تم تحضير العديد من تركيزات معامل الهلام عن طريق إذابة الدواء في الزيت عند درجة حرارة ٨٥ درجة مئوية، وإضافة palmitic acid مع التحريك المستمر لمدة ٤٠ دقيقة للحصول على محلول شفاف، ثم ترك الخليط ليصل إلى درجة حرارة الغرفة (24±2°C) ليتصلب. تم إعداد الصيغ وتقييمها بناءً على مظهرها الفيزيائي، ودرجة الحرارة الأنتقالية، وقابلية الانتشار، واللزوجة، ودرجة الحموضة، ودراسة تحرير الدواء خارج الجسم، ودراسة قابلية التضاد الفطري، وصورة المجهر الألكتروني النافذ واختبار تهيج الجلد مع الفحص النسيجي. أجريت دراسة التوافق باستخدام مطيافيه الأشعة تحت الحمراء لتحويل فوريه (FT-IR) حيث أظهرت الدراسة أن لايوجد تداخل بين الدواء والسواغات. جميع التركيبات المصممة من الفوريكونازول تظهر خصائص فيزيائية مقبولة، ودرجة حرارة تحول المحلول الى هلام والهلام الى محلول مناسبة ودرجة الأس الهيدروجيني المناسبة للجلد. أظهرت دراسات اللزوجة والانسيابية سلوك ترقق القص البلاستيكي الزائف للجيلات العضوية. من بين جميع التركيبات،يظهرpalmitic acid مع زيت بذور العنب تحريرا أفضل للدواء من أجل توصيل الدواء الموضعي بشكل مستدام؛ من النتائج المذكورة أعلاه أن palmitic acid مع تركيبة زيت بذور العنب قد يكون خيار علاج موضعي واعد لعلاج الالتهابات الفطرية الجلدية.

الكلمات المفتاحية: فوريكونازول ، حامض زيت النخيل،هلام عضوي، زيت بذور العنب، معامل الهلام.