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# Development and *in vitro* evaluation of griseofulvin cream formulations for the treatment of *Tinea pedis*

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## Abstract

**Background**: Tinea pedis, commonly known as athlete's foot, is a widespread fungal infection of the feet affecting children and adults across Africa, including Tanzania. Traditionally, oral griseofulvin tablets have been the mainstay of treatment. However, oral administration is often associated with systemic side effects, particularly in children. There is a growing need for localized, safer, and more tolerable treatment alternatives. Developing a topical formulation of griseofulvin offers a promising approach to directly target the infection site while minimizing systemic exposure and associated adverse effects.

**Objective**: To formulate and evaluate a topical griseofulvin cream as a safer and more effective alternative to oral administration for treating Tinea pedis.

**Methodology**: Four griseofulvin cream formulations were developed Using standard pharmaceutical excipients (F1, F2, F3, and F4). The formulations underwent comprehensive in vitro evaluation, including Viscometry, frequency sweep, three-step shear rate tests, and creep and recovery analysis, which were conducted to assess the flow behavior and consistency of the creams.

Accelerated stability testing was performed over 90 days at 40°C ± 5°C and 75% ± 5% relative humidity. The formulations were evaluated for physical stability and active ingredient assay.

F3 was tested against Trichophyton rubrum to determine antifungal efficacy. Skin tolerance was assessed by scoring erythema and oedema responses

**Results**: Formulations F1, F2, and F3 demonstrated favourable rheological properties, with F3 exhibiting the most consistent and desirable flow characteristics. F4 showed suboptimal behavior and was excluded from further consideration.

All formulations remained stable over 90 days, with minor assay variations (100.62% on day 0 to 99.68% on day 90), indicating excellent formulation stability. F3 showed strong antifungal activity, producing a 37.7 mm zone of inhibition against Trichophyton rubrum. The irritation potential of F3 was minimal, with average oedema and erythema scores of 1.17, indicating good skin compatibility.

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**Conclusion**: The study successfully developed a stable and effective griseofulvin topical cream. F3 emerged as the most promising candidate among the formulations due to its superior rheological properties, potent antifungal activity, and excellent skin tolerance. This topical cream offers a safer alternative to oral griseofulvin for treating Tinea pedis, particularly among school-aged children.

**Keywords;** Griseofulvin; Cream; Rheological properties; Physical appearance; pH; Antifungal activity.

## 1. Introduction

Dermatological conditions, especially fungal skin infections, pose a significant global health concern, particularly in sub-Saharan Africa. Topical therapy offers considerable benefits in managing these infections by enabling targeted drug delivery directly to the affected skin areas while minimising systemic side effects. Developing an effective topical cream involves careful selection of excipients, especially emulsifiers, which are crucial in modifying the thermodynamic properties of the active ingredient, griseofulvin. Such modifications improve drug dispersion through the skin, overcoming physical barriers and facilitating deeper penetration.

The choice of emulsifiers, based on their Hydrophilic Lipophilic Balance (HLB) values, is vital for determining the cream's viscosity. Precise calculation and appropriate selection of emulsifiers are essential to prevent undesired liquid crystalline phases, thereby ensuring the cream's consistency and stability.

The griseofulvin cream exhibits complex rheological behaviours, characterised by reversible shear breakdown, viscoelasticity, and thixotropy. Understanding these properties provides valuable insights into the performance of the semisolid dosage form regarding storage, stability, spreadability, and skin penetration.

In this study, a series of rheological assessments were performed on various formulations of griseofulvin cream, including viscometry (flow curves), yield point determination (ramp test), frequency sweeps (oscillatory tests), three-step shear rate tests, and creep and recovery analyses. These evaluations helped identify distinct characteristics across four pharmaceutical-grade formulations.

Currently, griseofulvin is not registered in semisolid dosage forms in Tanzania. Treatment of Tinea pedis primarily relies on oral griseofulvin tablets. Oral administration is associated with significant side effects, dosage complications, and compliance challenges, especially among primary and secondary school children. Furthermore, griseofulvin's poor aqueous bioavailability and limited water solubility make it ideally suited for topical applications due to its lipophilic nature. The drug is classified as Class II in the Biopharmaceutical Classification System.

Therefore, developing a topical cream formulation offers considerable benefits, including reduced systemic toxicity and improved patient compliance compared to oral therapy. Consequently, topical delivery provides a promising alternative therapeutic approach to address the limitations of oral griseofulvin. administration.

## 2. Materials and Methods

### 2.1. Materials

Griseofulvin of analytical grade was supplied by Korea Chemical Ltd, while Polysorbate 80 (Tween 80) with an HLB of 15 was sourced from Sigma Aldrich (Switzerland). Sorbitan oleate (Span 80) (HLB = 4.3) was obtained from Sigma (USA), and White Vaseline (hlb = 5) was provided by Caesar and Loretz Gmbh. Distilled water was acquired from the University of Bergen (UiB), and Toluene, diethyl ether, ethyl acetate, albino rats, potato agar, and Trichophyton rubrum, along with the incubator, were available at Muhimbili University of Health Sciences and Allied Sciences, Dar es Salaam, Tanzania.

### 2.2. Method

#### *2.2.1. Preparation of the Formulations*

The experimental study involved the preparation of formulations (F1-F4) containing 10% (w/w) griseofulvin. For formulation F1, purified water was heated to approximately 50 °C, while griseofulvin was liquefied at 70 ° C. Polysorbate 80 (Tween 80), sorbitan oleate (Span 80), and Vaseline were separately melted at around 70 °c. The griseofulvin-water mixture was then combined with the melted excipients and homogenised at 4200 rpm for 10 minutes, resulting in a transition from translucent to a rich white colour, indicating reduced droplet size and improved stability. Care was taken

to avoid introducing air during mixing. The formulation was allowed to cool naturally to 30°C, transferred to airtight containers, and stored for at least 48 hours before conducting physical, rheological, pH, and stability testing. The same procedure was followed for formulations F2, F3, and F4, as shown in Table 1.

**Table 1** Formulations of Griseofulvin cream 10% (w/w)

| | **Weight (g) F1** | **F2** | **F3** | **F4** |
|---|---|---|---|---|
| Ingredients | | | | |
| Griseofulvin | 5.041 | 5.04 | 5.06 | 5.07 |
| Polysorbate 80 (Tween80) | 0.2548 | 0.259 | 0.259 | 0.256 |
| Sorbitan oleate (Span80) | 1.252 | 1.257 | 1.254 | 1.256 |
| Vaseline | 23.52 | 28.53 | 33.52 | 38.51 |
| Purified water | 20.3 | 15.4 | 10.4 | 5.09 |
| Total (grams) | 50.368 | 50.486 | 50.493 | 50.182 |

*2.2.2. Rheological Characterisation*

Rheological analysis of the formulations was conducted using a stress-controlled rheometer, specifically a Kinexus Netzch rheometer equipped with a CP geometry spindle CP4/40 SR1454SS (KJ3100277). A Peltier hood maintained the sample temperature at 25 °C and minimised evaporation during testing. The appropriate amount of GF cream was carefully placed on the plate, and a stainless-steel spatula was used to trim any overfilled cream to prevent additional stress from dragging along the edges. Approximately 10 g of each formulation was applied to the lower plate, and the upper plate was lowered to a fixed gap of 100 µm. A steady-state flow test was conducted over a shear rate range of 0.1 to 100 $s^{-1}$ to evaluate flow behaviour. Viscosity values were recorded at 0.100 $s^{-1}$ up to an end shear rate of 100.0 $s^{-1}$.

Dynamic oscillatory testing was conducted to further investigate the viscoelastic properties. After identifying the linear viscoelastic region (LVR) through strain sweep, a frequency sweep was performed across an angular frequency range of 10Hz to 0.1Hz, with shear stress ranging from 0.00Pa to an end shear stress of 200Pa, while maintaining shear strain at 0.5, and varying from 0.1 to 100 rad/s to characterise the microstructural behaviour of the formulations.

*2.2.3. pH Measurement*

The pH of each formulation was measured using a calibrated pH meter. Calibration was performed with standard buffer solutions of pH 4.0, 7.0, and 10.0. Approximately a sample of each formulation was placed in a suitable container and gently tapped to eliminate entrapped air. The pH was recorded for each sample, and the electrode was rinsed with deionised water followed by 70% v/v ethanol between measurements to prevent cross-contamination.

*2.2.4. Accelerated Stability Study Using HPTLC*

A three-month accelerated stability study was conducted to assess the chemical stability of the griseofulvin cream formulations. The analysis was performed using a High-Performance Thin-Layer Chromatography (HPTLC) method developed and validated in-house by the Research and Development Department at Muhimbili University of Health and Allied Sciences. The formulations were stored under accelerated conditions in accordance with ICH guidelines. At predetermined intervals over the three months, samples were collected and analysed using HPTLC to quantify griseofulvin and identify any potential degradation products.

*2.2.5. In Vitro Antifungal Activity by Agar Plate Diffusion Method*

The antifungal activity of the griseofulvin cream formulations was evaluated using the agar plate diffusion method. Potato Dextrose Agar (PDA) served as the growth medium due to its suitability for cultivating dermatophytes and other fungal species. Agar plates were prepared under sterile conditions and inoculated with Trichophyton rubrum.

A sterile cork borer created wells of 15 mm diameter in the solidified agar. Approximately 100.2 mg of each cream formulation was accurately weighed and aseptically introduced into the wells. The plates were then incubated at 28 ± 2 °C and observed over five consecutive days to monitor the zone of inhibition. The antifungal activity was assessed by measuring the diameter of the clear zone (zone of inhibition) around each well at regular intervals.

*2.2.6. Skin irritation test*

The study evaluated the dermatological tolerance and potential irritation of the formulated cream using healthy adult albino mice. It involved the topical application of the formulation to the shaved dorsal area of each animal under standardised conditions. Observations were recorded for signs of erythema, oedema, or other skin reactions over three consecutive days following application. Scoring was performed daily based on a standardised dermal irritation scale, and the results were utilised to assess the formulation's stability and safety profile under physiological conditions.

### 2.3. Statistical Analysis

All the data were statistically analyzed by Microsoft Excel 2010 and rSpace Software 2.

## 3. Results

The rheological properties of griseofulvin cream formulations (F1-F4) were assessed and compared using various methods, including viscosity evaluation (flow curves), frequency sweep analysis (oscillatory or fingerprint spectra), shear stress ramp tests (to determine yield stress), and thixotropy assessments (to examine the uniformity of griseofulvin distribution within the cream). Additionally, creep and recovery tests were conducted to evaluate deformation characteristics. Further investigations included pH measurements, stability studies, antifungal activity tests, and skin irritation assessments.

### 3.1. Rheometry

*3.1.1. Viscometry-Flow Curve*

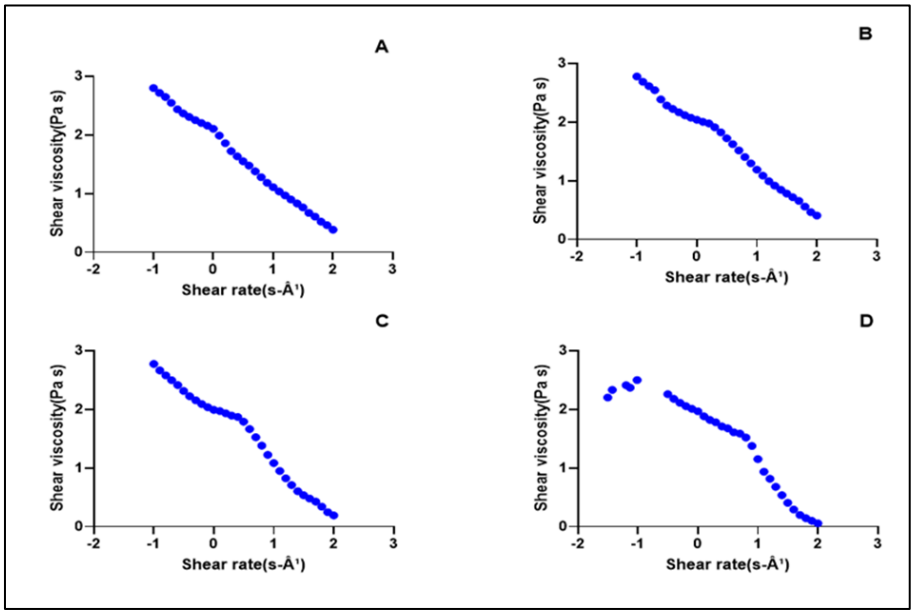


**Figure 1** Viscosity versus shear rate for different topical griseofulvin formulations. Formulations F1, F2, and F3 demonstrated a clear curve with distinct zero shear viscosity and yield stress, as shown in Fig. 1A, B, and C (with F3 displaying the best optimal results), while Formulation F4 exhibits distortion as the shear rate approaches zero (Fig. 1D)

Viscosity curves were generated for the four griseofulvin formulations at 25°c. The flow curves were conducted in both upward and downward directions, beginning with a shear rate of 0.100 $s^{-1}$ and concluding at a shear rate of 100.0 $s^{-1}$. Figure 1 displays the shear rate viscometry results for the four formulations, which were obtained using the Kinexus rheometer analysis with rSpace software version 2.1(1). The formulations demonstrate shear-thinning behaviour, where their viscosity decreases as the shear rate increases. In regions of zero shear viscosity, the viscosity maintains a plateau as the shear rate approaches zero, while the yield stress suggests an increasing viscosity as the shear rate nears zero.

This indicates that the F4 cream formulation is more complex during application and requires more strength to spread and disappear into the skin. The formulations demonstrated non-Newtonian fluid behaviour. This formulation had a

high solid content (griseofulvin and vaseline). Consequently, the low shear rate viscosity region vanished between shear rates of 0.1 and 1 ($s^{-1}$).

*3.1.2. Oscillatory-Frequency Sweep*

The curve provided a comprehensive overview of the formulations' behaviour during storage and application to the affected skin area, detailing the fingerprint spectrum of the Griseofulvin cream. The frequency sweep for the formulations is presented in Figure 2. In formulation F1 (Figure 2A), the elastic modulus (G') was more significant than the viscous modulus (G'') at low frequencies (<1 Hz), indicating that the cream exhibited viscous properties with a network structure that required breakdown before flow initiation. This behaviour suggests the presence of yield stress.

For formulation F2 (Figure 2B), the G' modulus was marginally greater than G'', suggesting that the formulation preserved its viscous properties.

In formulation F3 (Figure 2C), the elastic modulus (G') and viscous modulus (G'') intersect at a frequency of 10 Hz, which is significantly higher than the standard 1 Hz. This crossover indicates favourable semi-solid characteristics, suggesting good long-term storage stability. The cream exhibits a balanced elastic and viscous behaviour, which is essential for maintaining structural integrity within the container. Its internal structure effectively stores and dissipates energy, maintaining a state of equilibrium.

For formulation F4 (Figure 2D), G' was less than G'' at low frequencies (<1 Hz), indicating that the cream primarily displayed elastic properties.

The phase angle analysis highlighted the viscoelastic nature of the formulations. For F1, F2, F3, and F4, the phase angle remained slightly above 0° with a minor reduction at lower frequencies, indicating that the cream behaved as a viscoelastic solid at 0 Hz.

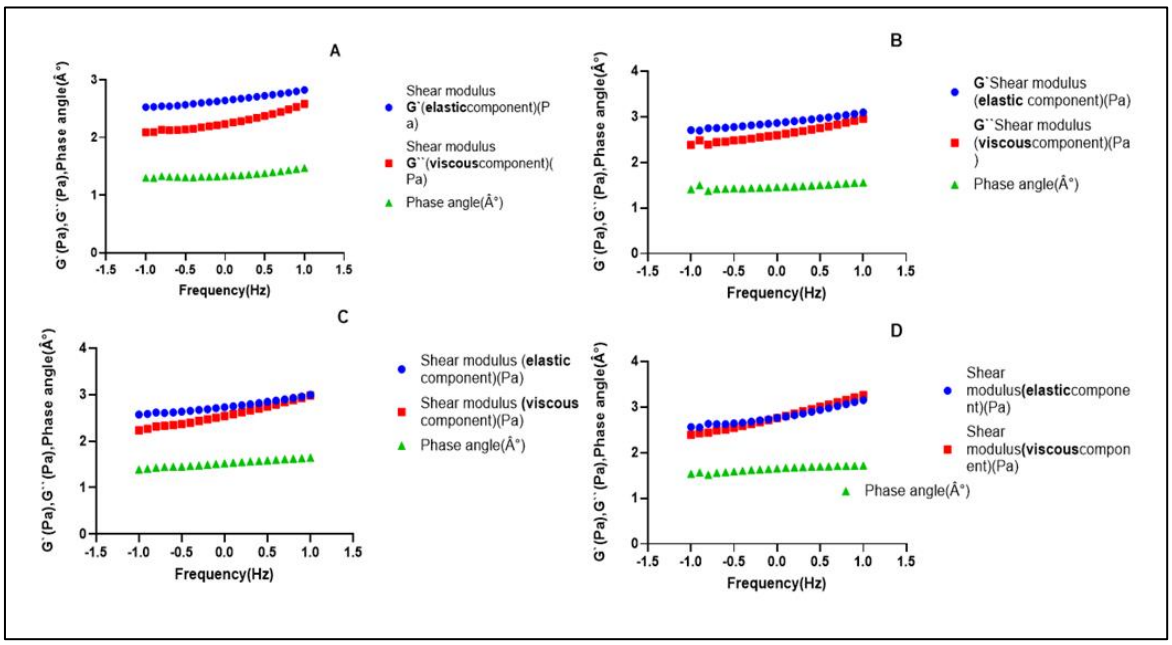


**Figure 2** The relationship between elastic modulus, viscous modulus, and phase angle versus frequency was analyzed for topical griseofulvin formulations (F1, F2, F3, and F4). In Figure 2A, the formulation F1 exhibited viscous properties indicative of a network structure. Figure 2B, F2 demonstrated a predominantly viscous behaviour. Figure 2C, F3 highlighted shear stress values corresponding to desirable semi-solid properties, ensuring stability over an extended storage period. Meanwhile, Figure 2D, F4 revealed that the cream primarily exhibited elastic characteristics

*3.1.3. Thixotropy*

The results for the three-step shear rate were used to study and evaluate the formulated griseofulvin cream regarding the time required to recover 90% of the defined amount from the initial viscosity at 25°c. The first stage featured a low shear rate of 0.5Pa, which demonstrated the cream's rest state, producing a clear curve for the first phase. This was

succeeded by the second stage, which employed a high shear rate of 100Pa over a designated time, resulting in the breakdown of the cream's structure, comparable to the process of interest. Lastly, the third stage repeated the same low shear rate of 0.5Pa as the first.

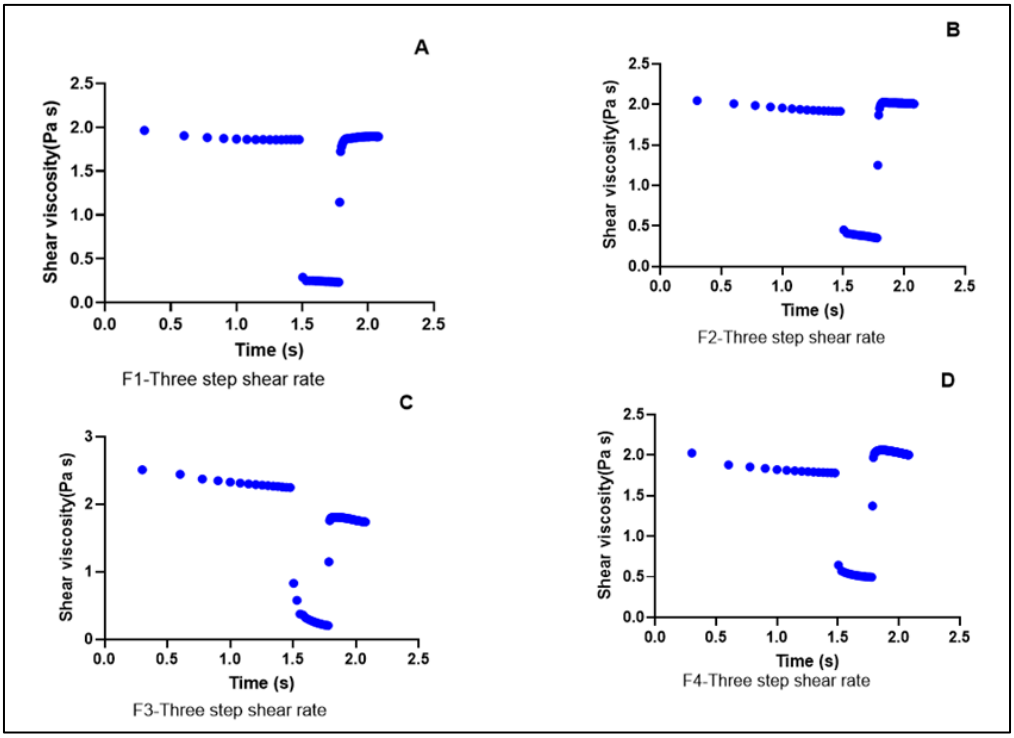


**Figure 3** The three-step shear rate assessment revealed the thixotropic behaviour of the griseofulvin formulations F1, F2, F3, and F4. In Figure 3A, formulation F1 exhibited lower thixotropy due to its higher water content, resulting in a less structured internal matrix. Formulation F2, displayed in Figure 3B, also demonstrated relatively low thixotropic properties. In contrast, formulation F3 (Figure 3C) exhibited significantly improved thixotropic behaviour, characterised by an optimal recovery time, regaining approximately 90% of its initial viscosity. Conversely, formulation F4 (Figure 3D) showed the lowest thixotropic properties among all the formulations tested.

*3.1.4. Creep and recovery test*

The consistency of each formulation was assessed using a range of stresses both below and above the stress ramp (yield stress). Furthermore, creep and recovery tests were performed to ascertain the viscoelastic properties of the formulations. Compliance (J), defined as the reciprocal of modulus (J = 1/G = strain/stress), was automatically calculated using the Kinexus rheometer software, where G represents modulus and γ indicates strain. The creep test involved applying very low stresses to generate curves illustrating strain or compliance over time. Table 2 summarises the minimum stress values required to produce creep curves during the analysis.

**Table 2** Stress ramp(Pa) for compliance verse time.

| Formulae | Stress Ramp (Pa) | Lowest stress (Pa) |
|---|---|---|
| F1 | 7.15 | 6 |
| F2 | 6.143 | 5 |
| F3 | 4.944 | 4 |
| F4 | 4.193 | 3 |

The high value of creep compliance indicated that a formulation possessed a weaker internal structure. The equilibrium compliance assesses the viscoelastic formulation's elastic response to strain. The elastic reformation value reflects the elastic component of the viscoelastic behaviour. Thus, formulation F4 was found to be stable and consistent, with the

lowest stresses of 4 Pa and 5 Pa, respectively, corresponding to stress ramps of 4.944 Pa and 6.143 Pa obtained from the Kinexus rheometer.

*3.1.5. Compliances value verse Time(s)*

The compliance values plotted against time (s) demonstrate how the formulation reacts to stress, highlighting its viscoelastic properties. Initially, the compliance value gradually increases as the cream deforms under the applied stress. Formulations exhibiting lower compliance over time tend to possess greater structural integrity and enhanced stability, whilst those with higher compliance display more fluid-like behaviour and a weaker internal structure.

In Figure 4, the main region of the curve represents the initial compliance of each formulation. Formulation F1 (Figure 4A) displayed a compliance of 6 Pa-A, demonstrating sufficient stress to induce deformation and compromise the internal structure of the cream, followed by a series of parallel curves. Formulation F2 (Figure 4B) complied at 5 Pa-A, Formulation F3 (Figure 4C) at 3 Pa-A, and Formulation F4 (Figure 4D) at 2 Pa-A. Formulation F4 showed a gradual decrease in compliance due to strain hardening. The minimum acceptable compliance range was between 3 and 5 Pa-A, rendering Formulations F2 and F3 the most appropriate for compliance.

In the secondary region (steady-state deformation), the longest and most linear curve indicated a competitive balance between strain hardening and recovery. However, Formulation F4 (Figure 4D) exhibited breakpoints within the secondary region and a rapid rise in the curve at high shear over a short duration, suggesting a shorter deformation period, followed by Formulation F3 (Figure 4C). The tertiary region provided insights into microstructural changes, such as necking, accelerated deformation, or internal cracks(2).

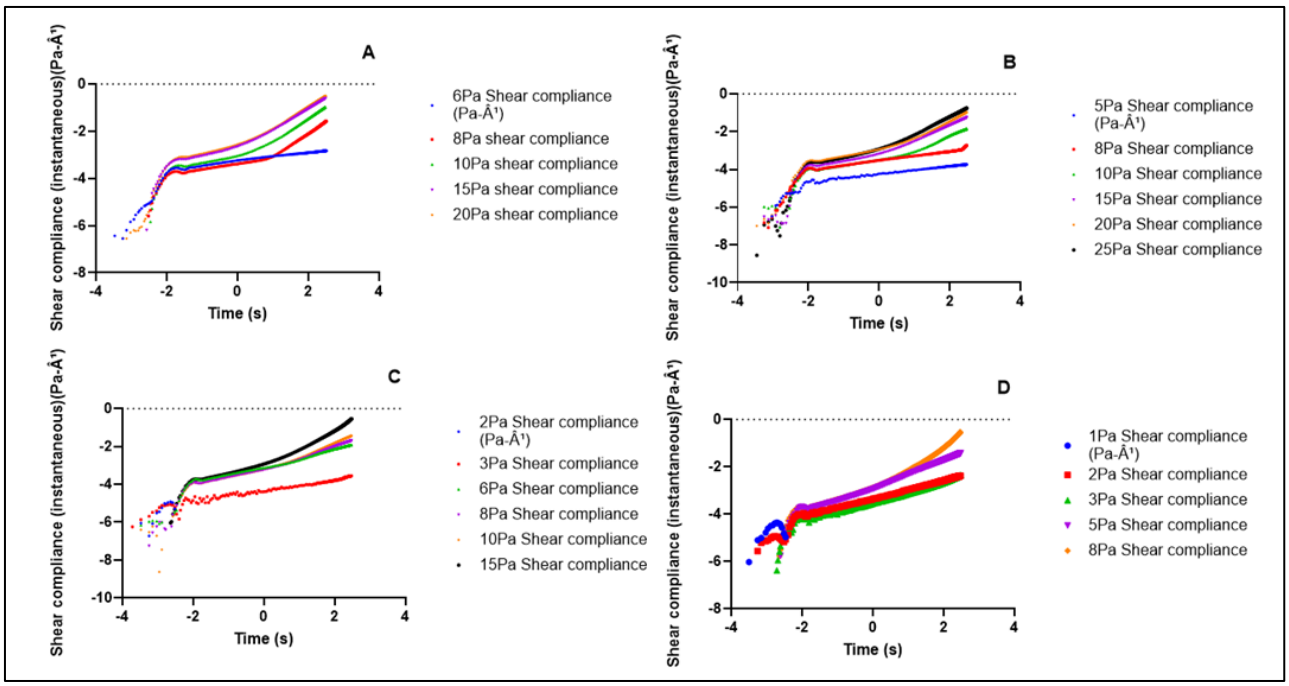


**Figure 4** F1 (Figure 4A), the curve crept immediately at 8 $Pa^{-1}$, without a preceding parallel line. Formulations F2 (Figure 4B) and F3 (Figure 4C) both exhibited creep at 10 $Pa^{-1}$, while Formulation F4 (Figure 4D) crept at 8 $Pa^{-1}$. These compliance values indicate the specific stress levels at which microstructural changes occur, marking the initiation point of deformation for each griseofulvin cream formulation.

### 3.2. Physical appearance and pH

The pH of the formulated creams was initially measured two days after preparation and subsequently monitored at intervals of 0, 30, 60, and 90 days to assess stability over time. Table 3 recapitulates the findings from physical assessments, including observations of colour and homogeneity and pH measurements. Throughout the study, all parameters consistently met the established quality standards, confirming that the formulations maintained appropriate physicochemical stability and uniformity during the evaluation period.

Table 3 Physical and pH properties for the four formulations at 40 °C ± 5 °C and a humidity of 75 ± 5% evaluated over 0, 30, 60, and 90 days.

Table 3 presents the physical appearance and pH values of the formulated creams. All formulations exhibited acceptable physical characteristics, including uniformity, smooth texture, and homogeneity, without signs of phase separation or discolouration. The pH values of all formulations were within the normal dermal compatibility range (typically 4.5–6.5), indicating their suitability for topical application without the risk of skin irritation.

**Table 3** Physical and pH properties for the four formulations

| **Parameter** | **Color** | | | | **Homogeneity** | | | | **pH** | | | | **Cracking** | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Formulation | F1 | F2 | F3 | F4 | F1 | F2 | F3 | F4 | F1 | F2 | F3 | F4 | F1 | F2 | F3 | F4 |
| 0 day | C | C | C | C | C | C | C | C | 6.4 | 6.7 | 6.5 | 7 | C | C | C | C |
| 30th day | C | C | C | C | C | C | C | C | 6.6 | 6.4 | 6.9 | 6.9 | C | C | C | C |
| 60th day | C | C | C | C | C | C | C | C | 6.8 | 6.7 | 6.8 | 7 | C | C | C | C |
| 90th day | C | C | C | C | C | C | C | C | 6.6 | 6.6 | 6.8 | 7.1 | C | C | C | C |
| Specification | White | | | | Homogenous | | | | 5-8 | | | | Non-cracking | | | |

The analysis of four griseofulvin formulations (F1, F2, F3, and F4) aimed to quantify the drug content and assess uniformity. Each formulation was analysed using appropriate analytical techniques, such as UV-visible spectroscopy or high-performance liquid chromatography (HPLC). The results indicated that all formulations contained drug content within the acceptable range, typically between 90% and 110% of the labelled claim, confirming accurate formulation and efficient incorporation of griseofulvin. F3 exhibited the highest uniformity and consistency in drug content among the tested formulations, indicating superior suitability for topical delivery. Figure 5 demonstrates the trends observed during accelerated stability studies from 0 to 90 days at a temperature of 40 °C ± 5 °C and a humidity of 75 ± 5% for the formulation.

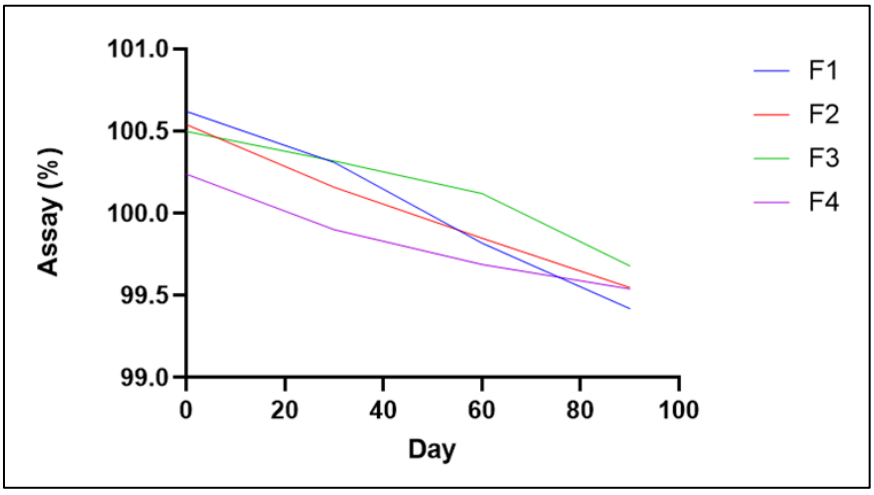


**Figure 5** Stability curve indicating percentage assay against the number of days, showing optimal trends of 100.62% to 99.68%, in which F3 of griseofulvin cream was found to be more stable

### 3.3. Antifungal activities

Both formulations exhibited significant inhibitory effects against Trichophyton rubrum, the fungus responsible for Tinea pedis. Among the formulations tested, formulation F3 demonstrated the strongest antifungal efficacy. After five days of incubation, clear inhibition zones were observed, with formulation F3 (Figure 6) showing the largest average zone diameter of approximately 37.5 mm. This substantial zone size underscores the potent antifungal potential of formulation F3, indicating its effectiveness in preventing fungal proliferation. The superior activity of formulation F3 is likely due to optimal drug dispersion, improved rheological properties, and enhanced drug release, making it particularly suitable for the topical treatment of fungal infections.

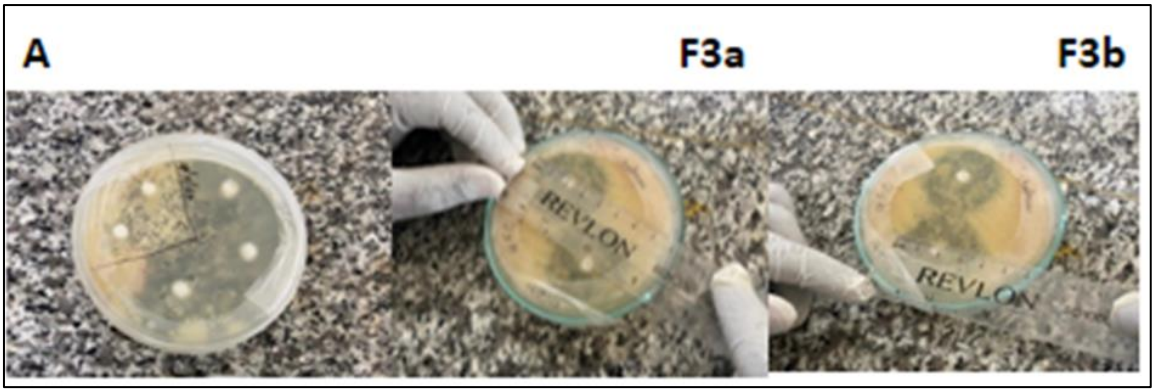


**Figure 6** Antifungal Activity of Griseofulvin Cream Formulations against *Trichophyton rubrum*. Fig 6A shows the control group (without the active formulation), while Fig. 6F3a and 6F3b present duplicate trials (*n=2*) of formulation F3. These trials demonstrate consistent and significant antifungal activity. The clear zones of inhibition observed for formulation F3 indicate effective suppression of *T. rubrum* growth compared to the control, confirming the formulation's potent antifungal properties

### 3.4. Skin irritation test

Formulation F3 demonstrated minimal skin irritation, with average scores for oedema and erythema recorded at 1.17 following three consecutive days of observation (Table 4). This low irritation score indicates that formulation F3 is well tolerated and suitable for topical application, suggesting a favourable safety profile for potential therapeutic use.

**Table 4** Skin irritation scores (edema and erythema) for albino mice observed over 72 hours

| Time (Hrs) | Mouse ID | Edema score | Erythema Score |
|---|---|---|---|
| 24 | 0 | 0 | 0 |
| | I | 1.5 | 1 |
| | II | 1 | 1.5 |
| | III | 1 | 1 |
| 48 | 0 | 0 | 0 |
| | I | 1.5 | 1.5 |
| | II | 1.5 | 1.5 |
| | III | 1 | 1 |
| 72 | 0 | 0 | 0 |
| | I | 1 | 1 |
| | II | 1 | 1.33 |
| | III | 1 | 1 |
| Average Score | | 1.17 | 1.17 |

*Note*: Mouse labeled "0" represents the control group. Both edema and erythema were evaluated on a scale from 1 (very slight, barely perceptible) to 4 (severe edema or erythema).

## 4. Discussion

The rheology and physical properties of griseofulvin cream were evaluated during the first two days after formulation. The physical properties were observed to meet the acceptance criteria: white colour, homogeneity, and non-cracking. Rheological tests for the four formulations exhibited distinct characteristics.

The three-step shear rate characterization of the formulations demonstrated a complex rheological property typical of non-Newtonian flow. Shear thinning was observed across the four formulations with varying thixotropic levels. This indicates that the Griseofulvin cream exhibited thixotropic behaviour, characterised by a complete reduction and degradation of structural strength during the shear-load phase.

Formulation F3 exhibited suitable thixotropic properties, with 90% regaining of initial viscosity, enabling it to be applied and spread on affected skin, where increased rubbing (thinning) would allow the drug to penetrate the skin. Viscosity of the formulations over time indicated the ageing and storage time (shelf life), in which the viscosity increased or hardened with increasing time, as in the case of monitoring the change in G`(elastic structure) over time(3,4).

The griseofulvin cream's frequency sweep and oscillatory test revealed a stable fingerprint spectrum and a well micro-structured arrangement. This structure plays a significant role in the storage of the cream. Among the formulations tested, formulation F3 exhibited a good and well-balanced cream, which can also be used as a formulation tool to assess the performance of semisolid dosage forms during storage and their stability and spreadability when applied to infected skin.

Determining the linear viscoelastic spectrum in an oscillatory test required using a trimmed stress level to ensure consistency in the formulation. In this test, variations were observed due to low consistency, as using small stress levels within the linear viscoelastic region can be challenging for oscillatory tests. To address these variations, the optimal viscoelastic properties of Griseofulvin cream were determined through a creep and recovery test. This involved applying a constant stress derived from the lowest ramp number among the four formulations (below the yield stress) and a specific time interval. The viscoelastic results from the frequency sweep oscillatory test demonstrated that the formulated Griseofulvin cream exhibited a lamellar phase-like microstructure. This test also aided in optimising the ratio of water and petroleum jelly (Vaseline) to selected emulsifiers, as well as enhancing the physical stability, consistency, and homogeneity of the formulation(5)

The results from the frequency sweep showed an optimal impact on the physical properties and availability of Griseofulvin to the affected and target regions of the patient`s skin. It also demonstrated that the technique used during formulation was optimal and led to an elegant formulated cream.

The stress ramp in cream formulations F3 and F2 demonstrated shear stress ramps with predominant, appropriate solid-like properties that maintained the network's integrity, thus being related to the yield stress. The viscosity peak at which the cream underwent elastic deformation and stretching indicates that the cream can be easily squeezed, applied, and spread on the skin.

In the creep and recovery test, formulations F1 and F4 exhibited low creep equilibrium compliance, suggesting weaker internal structure, as shown in the tertiary region of the curve. This was subsequently followed by F2 and F3, which showed higher compliance, indicating that it will take longer for the microstructure to change(5)The creep compliance test was done at 25 °C with variable stress ramps, as indicated above. Thus, the studied rheological parameters can also be employed in the preliminary preparation and formulation of specifications in accordance with regulatory guidelines.

The pH of the Griseofulvin cream was found to range from 5.5 to 6 in the first two days following the formulation of the cream. Meanwhile, the accelerated stability test ranged from 6 to 7 from day 0 to 90, with a notable decrease in pH to 6.1 for formulation F1 and an increase in pH to 7.1 for formulation F4, indicating the dynamic changes in pH within the formulations (6). The pH of the creams remained within the accepted criteria

The accelerated stability assessment using a high-performance thin-layer chromatographic method for identifying and quantifying griseofulvin cream demonstrated that the formulations were significantly stable. Formulation F3 exhibited the greatest stability, as indicated by the area under the curve and trend graphs for the four formulations. The percentage trend ranged from 100.68% on day 0 to 99.68% on day 90.

Antifungal activity of Griseofulvin cream for formulation F3 had shown a powerful activity against *Trichophyton rubrum* with a zone of inhibition of 37.5mm(7). The skin irritation effect of the cream was very slight, with an average Edema and Erythema score of 1.17(8).

Moreover, the choice of formulation type, based on the water-to-Vaseline ratio, had significant implications for cost-effectiveness, especially when scaling up production in developing countries.

## 5. Conclusion

This study developed the first semisolid griseofulvin formulation in Tanzania, focusing on its rheological properties, pH stability, antifungal efficacy, and potential for skin irritation. Among the four formulations tested, formulation F3 showed the best rheological behaviour, stable pH, and significant antifungal activity against *Trichophyton rubrum*, the organism responsible for Tinea pedis. Additionally, the cream demonstrated minimal skin irritation, indicating good tolerability. Further studies are recommended to evaluate the antifungal effectiveness against other causes of Tinea capitis, such as *Trichophyton tonsurans*, *T. violaceum, T. soudanense*, and *Microsporum canis*.

## Compliance with ethical standards

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Disclosure of conflict of interest

No conflict of interest to be disclosed.

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