Spectroscopic and method validation studies of Terbinafine hydrochloride in spray form

Nadia Mumtaz[1], Freeha Hafeez[1*], Muhammad Suleman[1], Abrar Ahmad Anjum[1], Muhammad Bilal[1]

[1]Department of Chemistry, Riphah International University Faisalabad

Abstract:

Objective: Terbinafine hydrochloride (TFH) is an allyl amine derivative used to treat fungal infections like pityriasis versicolor, dermatophytosis, and tineacapitis. It inhibits squalenceepoxidase, an enzyme involved in fungal cell wall formation, leading to cell death. Terbinafine, the industry leader in topical antifungals, has captured 80% of the projected US$1.5 billion worldwide market for onychomycosis. Terbinafine is the only oral allylamine sold commercially, and other formulations have been added. This study evaluates the mycology and pharmacology of terbinafine, focusing on dermatophytosis and its role in non-dermatophyte infections.

Introduction: Terbinafine, an oral allylamine, has reached its 17-year mark worldwide in 2008. It has 80% of the global market for onychomycosis, worth over US$1.5 billion, and accounts for most prescriptions for children with the condition. The antimycotic therapy group has expanded its portfolio with new formulations, including an oral granule for paediatric patients in 2007 (Zhang et al., 2020). The study will evaluate the growing body of knowledge regarding terbinafine mycology and pharmacology, focusing on dermatophytosis and its role in non-dermatophyte infections. Its safety profile in humans is enhanced due to its high selectivity for fungal enzymes and minimal impact on cholesterol synthesis in mammals. However, terbinafine has not yet been developed for pesticide applications due to its non-toxicity.

Pathogenic fungi, known as dermatophytes, have a strong affinity for keratin found in skin, hair, and nails. dermatophytosis, but resistance to terbinafine is mostly undetected.

Terbinafine Hydrochloride (TH) is a strong antifungal drug used to treat superficial fungal infections of the skin and nails (Gaurav et al., 2021). It is almost the first active for the treatment of onychomycosis and is very successful in treating dermatophyte infections. Terbinafine Hydrochloride is a common allylamine antifungal medication used to treat dermatophyte infections and exhibits strong fungi. Jock itch, and Tineacruris. However, it is lipophilic and barely soluble in water, necessitating quickly dissolving tablets to promote quick release and start of action. Terbinafine Hydrochloride is commonly used topical and oral fungicidal medication effective against dermatophytes, but its potential side effects have been linked to severe cutaneous response, neutropenia, and liver failure when taken orally (Dwiecki, Michalak, & Muszalska-Kolos, 2022). Gel 5, a new drug delivery method, has been developed to address these issues. Onychomycosis is a common and incurable fungal infection, with oral antifungal medication being the preferred treatment due to its low drug penetration (Shivakumar, Vaka, Madhav, Chandra, & Murthy, 2010). However, side effects from oral delivery need to be addressed. Proliposomes offer a novel carrier-mediated drug delivery method, offering stability, flexibility, and convenience in transportation, distribution, storage, processing, and packaging. One such drug is terbinafine, which works best on Candida glabrata yeasts and Onygenales fungi. Topical antifungal medicines are often preferred over oral ones due to their self-administrability, safety, and ease of discontinuation. Topical administration ensures optimal drug release and penetration, but a higher oral dose increases the risk of side effects (Ryder & Leitner, 2001). Nanogels have shown promise as a promising nanoparticle drug delivery technology. This work aims to create pH-responsive gelatin and AA crosslinked nanogels for treating Dermatophytosis, focusing on their DEE, release, skin deposition, and antifungal activity. Onychomycosis, a fungal illness causing up to 50% of nail abnormalities, affects 3-23% of the US and European population, with higher prevalence among the elderly and those with diabetes. Risk factors include immunosuppression, poor peripheral circulation, nail damage, and tinea pedis. The aging population and the spread of AIDS and the human immunodeficiency virus are expected to increase the incidence of onychomycosis. Treatment with oral terbinafine and itraconazole has significantly improved, but many nail infections remain difficult to treat. Fungal diseases are common, with over a billion infections identified annually (AbdelSamie, Kamel, Sammour, & Ibrahim, 2016). Antifungal medications can effectively treat fungal infections, but they carry risks of serious side effects, such as liver damage, altered estrogen levels, and allergic reactions. Terbinafine hydrochloride, a fungicidal allylamine class medication, has a wide range of antifungal activity and inhibits squalenceepoxidase, leading to intracellular accumulation of toxic squalene and fungal cell death. Thydrochloride oral granules are a new paediatric formulation

that is easily ingested and sprinkled over food. Terbinafine hydrochloride (TF-HCl) is a synthetic allylamine antifungal medication used to treat superficial fungal infections of the skin and nails. Oral therapy is often used for scalp or nail infections (Vena, Micali, Santoianni, Cassano, & Peruzzi, 2005).

Experimental Work:

The study used HPLC and AR grade reagents and chemicals, including hydrochloric acid, sodium hydroxide, monobasic potassium phosphate, phosphateic acid, methanol, and acetonitrile, to formulate a spray formulation for terbisil and terbinafine. The spray was compressed in bi-layer form using a compression machine. Glassware and equipment were meticulously calibrated, cleaned, rinsed, and oven dried. Various organic and inorganic chemicals were used to develop an analytical testing method for simultaneous estimation of terbisil and terbinafine in spray form. The in vitro release profiles of active ingredients were evaluated using a 6 VDC system. The receptor media was prepared and degassed using 0.45 µm regenerated cellulose membranes under vacuum, followed by stirring for 2 minutes at room temperature . The analytical apparatus used for method validation and development were 21 CFR compliance, appropriately calibrated, and qualified. The model and brand names of instruments included an analytical weighing balance, bath sonicator, magnetic stirrer, pH meter, HPLC, UV-Visible spectrophotometer, dissolution apparatus, analytical balance, ultrasonic batch, and UV-VIS spectrophotometer. The UV-VIS spectrophotometer, auto-sampler HPLC system, and dissolution apparatus were all calibrated and qualified according to their manufacturer's specifications. The study aimed to develop a reliable and accurate analytical method for estimating terbisil and terbinafine in spray form.

Analytical Method Development: The process involves selecting a suitable detection wavelength, buffer, mobile phase, and stationary phase for terbisil and terbinafin. The chosen wavelength is determined using HPLC or UV-Visible spectrophotometer, and the mobile phase is chosen using appropriate chemicals and pH. The process involved weighing and transferring working standards of Terbisil and Terbisin HCl in a 100 mL volumetric flask. The active ingredient was dissolved with diluent-A and sonicated for 5-10 minutes. The resulting solution was then mixed with diluent-B, resulting in a final concentration of 0.01 mg/ml and 0.1 mg/ml for Terbisil and Terbisin, respectively. The sample solution was prepared by crushing 20 tablets into a fine powder, transferring 750 mg of sample to a 500 mL volumetric flask, and centrifuging for 5 minutes.

Calculation:

$$\%\ Assay = \frac{Avg.area\ of\ Sample}{Avg.area\ of\ Standard} \times \frac{Dilution\ of\ Standard}{Dilution\ of\ Sample} \times \frac{Avg.weight\ of\ tablet}{Label\ Claim} \times \%\ Purity$$

Dissolution: The study developed an analytical method for calculating Terbisil and Terbisin HCl in spray form using various dissolution media, including water and pH buffers. The 0.1N HCl solution was chosen as the most suitable. The procedure involved adding 900mL of dissolution media to six vessels, equilibrating the temperature, and running the apparatus for 30 minutes. The sample was filtered and the standard solution was prepared by dissolved Terbisil standards in dissolution media, followed by sonication and dilution. The final concentrations were 0.01 mg/ml and 0.1 mg/ml for Terbisil and Terbisin HCl, respectively.

Calculation

$$\%\ \text{Dissolution} = \frac{\boldsymbol{Area\ of\ Sample}}{\boldsymbol{Average\ area\ of\ Standard}} \times \frac{\boldsymbol{Dilution\ of\ Standard}}{\boldsymbol{Dilution\ of\ Sample}} \times\ \%\ \boldsymbol{Purity}$$

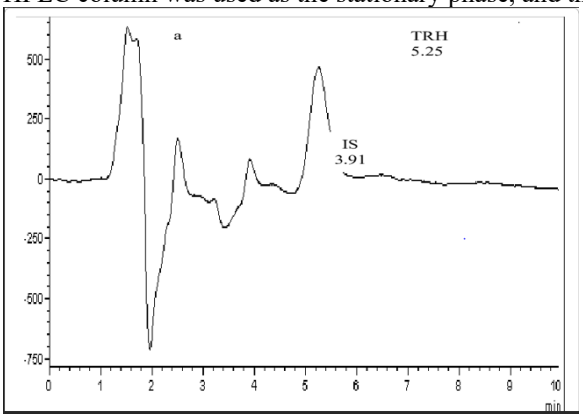
Result and Discussion:

Terbinafine hydrochloride (TFH) is an allylamine derivative that inhibits ergosterol synthesis by inhibiting squalene epoxidase, an enzyme involved in the growth of fungal and bacterial cell walls. It is used for treating skin infections like dermatophytosis, pityriasis versicolor, and cutaneous candidiasis, and superficial fungal infections like seborrheic dermatitis, tineacapitis, and onychomycosis. TFH is highly lipophilic and can accumulate in skin, nails, and fatty tissues, leading to side effects like allergic reactions, rash, vision changes, and blood problems.

Chemical Method: To an extent of Terbinafine Hydrochloride Spray, equal to 10 mg of Terbinafine Hydrochloride add methanol to make 10 ml, and use this answer as the pattern solution. Separately, dissolve 10 mg of terbinafinehydrochloride for assay in 10 mL of methanol, and use this answer as the fashionable solution. Spot 5 ml every of the pattern drug and well-known a plate of silica gel with fluorescent indicator for thin-layer chromatography. Develop the plate with the higher layer of a combination of eighty volumes of hexane, 20 volumes of ethyl acetate and 1 extent of ammonia answer (28) to a distance of about 15 cm, and air dry the plate. Examine below ultraviolet mild (main wavelength: 254 nm: the most important spot acquired from the pattern answer indicates the identical Rf fee with the spot received from the trendy solution.

Flow Rate	Adjust so that retention time of Terbinafine is about 8.5 min
Column Specification	ODS,5 µm (4.0mm X 125mm)
Column Temperature	constant temperature of about 25°C
Lamda Max	282nm
Diluent	Methanol
Injection volume	10micro Liter

Analytical Method Development: The method development process involved a literature review on the chemical and physical interactions between Terbisil and Terbisin HCl. The 80:10:10 MP combination with phosphate buffer, ACN, and alcohol was chosen as the stationary phase. The optimum composition for time- and cost-efficient procedures was achieved using the MP with a pH 4.0 buffer, ACN, and methanol (80:10:10). The C18 Welchrom HPLC column was used as the stationary phase, and the detector wavelength was adjusted to 210 nm.



Conclusion

- Analytical method development and validation are crucial steps in the pharmaceutical industry to ensure the quality, safety, and efficacy of drug products. In the case of Terbisil spray the development and validation of analytical methods are necessary to determine the quantity, purity, and identity of these active pharmaceutical ingredients (APIs) in the formulation.
- During method development, various parameters are optimized, including the mobile phase composition, column type, detection wavelength, flow rate, and sample preparation techniques. The aim is to achieve good separation, resolution, and sensitivity for the APIs. Additionally, method robustness, specificity, and linearity across the desired concentration range are assessed.
- Once an analytical method is developed, it needs to be validated to ensure its accuracy, precision, specificity, limit of detection (LOD), limit of quantification (LOQ), and ruggedness. Validation is typically performed according to guidelines provided by regulatory authorities such as the International Conference on Harmonization (ICH) or local regulatory agencies.
- The validated analytical method becomes an essential tool for routine quality control analysis of Terbisil spray. It ensures that the tablets meet the predetermined specifications for Terbinafine HCL and Terbisil content, which is crucial for maintaining consistent product quality and efficacy.
- In conclusion, the development and validation of an analytical method for Terbisil Spray involve selecting appropriate techniques, optimizing parameters, and assessing method performance. The validated method ensures accurate and precise quantification of the APIs, contributing to the quality control of the final product.

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