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# Simultaneous determination of terbinafine HCL and triamcinolone acetonide by UV derivative spectrophotometry and spectrodensitometry

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**Abstract**

A binary mixture of terbinafine hydrochloride and triamcinolone acetonide was determined by three different methods. The first one concerned with determination of both drugs using first derivative ($D_1$) spectrophotometric technique at 297 and 274 nm over concentration ranges of 5–30 and 4–24 μg $ml^{-1}$, with mean percentage accuracies $99.90 \pm 0.67$ and $100.25 \pm 0.49$, respectively. The second method depends on ratio-spectra 1st derivative ($RSD_1$) spectrophotometry at 298 and 248 nm over the same concentration ranges with mean percentage accuracies $100.22 \pm 0.51$ and $99.93 \pm 0.56$, respectively. The spectrodensitometric analysis provides a rapid and precise method for the separation and quantitation of both terbinafine hydrochloride and triamcinolone acetonide. The method depends on the quantitative densitometric evaluation of thin layer chromatogram of terbinafine hydrochloride and triamcinolone acetonide at 283 and 238 nm over concentration ranges of 5–25 and 2.5–22.5 μg $spot^{-1}$, with mean percentage accuracies $100.66 \pm 0.51$ and $100.27 \pm 0.73$, respectively. The suggested procedures were checked using laboratory prepared mixtures and were successfully applied for the analysis of their pharmaceutical preparations. The three methods retained their accuracy and precision when applying the standard addition technique. The results obtained by applying the proposed methods were statistically analysed and compared with those obtained by a reported method. 

*Keywords:* Terbinafine hydrochloride; Triamcinolone acetonide; Derivative spectrophotometry; Spectrodensitometry; Determination

## 1. Introduction

Terbinafine hydrochloride, (E)-*N*-(6,6-dimethyl-2-hepten-4-ynyl)-*N*-methyl-1-naphthalene methanamine hydrochloride (Fig. 1), is a new potent antifungal agent of the allylamine class that selectively inhibits fungal squalene epoxidase. The drug has broad-spectrum activity against yeast, fungi, molds and dermatophytes and is indicated for both oral and topical treatment of mycoses [1–4].

Terbinafine hydrochloride has been determined in biological fluids by high performance liquid chromatography [5–7] and microbiological

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bioassays [8,9]. Another HPLC method has been used to determine the drug in tablets and creams [10]. Ultra-violet (UV) spectrophotometric method was proposed for the determination of terbinafine hydrochloride in pharmaceutical formulation [11]. A voltammetric [12] and non-aqueous methods [13] have been reported for assay of the drug.

Triamcinolone acetonide is a glucocorticoid used mainly in the treatment of rheumatic disease and as an anti-inflammatory agent. It has a high oil-in-water partition coefficient, and for this reason, it is more often used in topical therapy [14].

Several methods were described for the determination of triamcinolone acetonide [15] such as polarography [16], visible and derivative spectrophotometry [17–20], HPLC [21–24] and gas chromatography [25]. British pharmacopoeia [26] and United States pharmacopoeia [27] described UV spectrophotometric methods. Terbinafine hydrochloride and triamcinolone acetonide are formulated in the form of ointment and cream, which were determined by HPLC [28].

Derivative spectrophotometry has been applied extensively to the simultaneous determination of substances with overlapping spectra, which is frequently made on the basis of zero-crossing measurements. Recently, a new spectrophotometric method for resolving binary mixtures was developed [29]. The method is based on the use of first derivative of the ratio spectra. The absorption spectrum of the mixture is obtained and divided (amplitudes at each wavelength) by the absorption spectrum of a standard solution of one of the components, and first derivative of the ratio spectrum is obtained.

The only method available for determination of the two drugs is HPLC [28], so there was a need to develop simple and accurate alternative methods that can be used for determination of the two analytes. The present work deals with simultaneous determination of terbinafine hydrochloride and triamcinolone acetonide by simple, rapid and selective derivative spectrophotometric and densitometric assays for quality control and routine analysis of the pure substances and in pharmaceutical preparations and may be able to eliminate the interference of excipients under optimal analysis conditions.

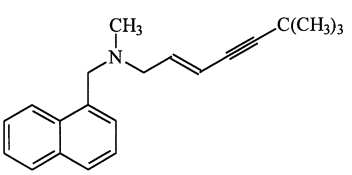


Fig. 1. Chemical structure of terbinafine, molecular weight = 291.44.

## 2. Experimental

### 2.1. Apparatus

1. All absorption spectra and derivatives were recorded with a Shimadzu UV-1601 PC. UV–visible double beam spectrophotometer with 1 cm quartz cuvettes, Shimadzu Corporation Kyoto-Japan.
2. Densitometer: dual wavelength Shimadzu flying CS-9000 with video display and high-speed, high-quality, parallel-head printer/plotter.
3. Hamilton micro-syringe, 25 μl, calibrated at 0.2 μl per unit.
4. Thin-layer chromatography (TLC) plates: precoated with Silica Gel GF, 0.25 mm thickness, fluorescent at 254 nm (E. Merck, Darmstadt, Germany).

### 2.2. Materials

#### 2.2.1. Samples

1. Triamcinolone acetonide was kindly supplied by Bristol–Myers Squibb Egypt. Its purity was found to be $100.49 \pm 0.45$ according to the British Pharmacopoeia method [26].
2. Terbinafine hydrochloride was kindly supplied by Novartis Pharma S.A.E. Cairo-C.C.R. 111108—under licence from Novartis Pharma AG., Basle, Switzerland. Its purity was found to be $99.88 \pm 0.65$ according to method [13].
3. Kenacort tablets (Bristol–Myers Squibb Co.); batch No. L92753. It was labelled to contain 4 mg triamcinolone acetonide/tablet.

4. Lamisil tablets (Novartis Pharma, Cairo, Egypt); batch No. B004 and B013. They were claimed to contain 125 and 250 mg terbinafine hydrochloride/tablet, respectively. The tablet excipients composed of colloidal silicon dioxide, hydroxypropyl methyl cellulose, magnesium streate, microcrystalline cellulose and sodium starch glycolate.
5. Lamisil cream 15 g (Novartis Pharma, Cairo, Egypt); batch No. B064. It was claimed to contain 10 mg terbinafine hydrochloride $g^{-1}$ of the cream. The cream base consists of cetyl alcohol, benzyl alcohol, cetyl palmitate, isopropyl myristate, polysorbate 60, purified water, sodium hydroxide, sorbitan monostearate and stearyl alcohol.

### 2.3. Reagents and solvents

All chemicals and reagents are of pure analytical grade. Methanol, dichloromethane and ether, all were obtained from El-Nasr Pharmaceutical Chemicals Co., Abu Zabaal, Cairo, Egypt.

### 2.4. Standard solutions

#### 2.4.1. Stock solutions

Terbinafine hydrochloride and triamcinolone acetonide stock solutions (1 mg $ml^{-1}$). Weigh accurately 100 mg of terbinafine hydrochloride and triamcinolone acetonide powder in two separate 100 ml measuring flasks. Add 25 ml methanol, shake for few minutes and complete to volumes with the same solvent. The stock solution of triamcinolone acetonide should be freshly prepared every day as in all such corticosteroids, is prone to oxidative rearrangement [15].

#### 2.4.2. Working solutions

Transfer 1 ml of each of the stock solutions of terbinafine hydrochloride and triamcinolone acetonide in two separate 25 ml measuring flasks and dilute to the mark with methanol to get a final concentration of 40 μg $ml^{-1}$ of both drugs for $D_1$ and ratio spectra 1st derivative ($RSD_1$) spectrophotometric methods; while using the stock solutions of terbinafine hydrochloride and triamcinolone acetonide, 1 mg $ml^{-1}$ in methanol for the spectrodensitometric method.

### 2.5. Laboratory prepared mixtures

1. For derivative spectrophotometric method and ratio spectra 1st derivative ($RSD_1$) spectrophotometric methods, transfer aliquot portion 1–9 of terbinafine hydrochloride from its working solution (40 μg $ml^{-1}$) into series of 10 ml measuring flasks. About 10–90% of triamcinolone acetonide using its prepared working solution (40 μg $ml^{-1}$) was added to the same flasks.
2. For densitometric method: Transfer aliquot portions equivalent to 2.5, 5–25 μg of terbinafine hydrochloride from its stock solution 1 mg $ml^{-1}$ to 5 ml measuring flasks. Add 10–90% of triamcinolone acetonide, using the prepared stock solution 1 mg $ml^{-1}$, to the same flasks.

### 2.6. Procedures

#### 2.6.1. First derivative ($D_1$) spectrophotometric method

*2.6.1.1. Construction of calibration curve*. Transfer accurately (1.25, 2.5–7.5 ml) and (1, 2–6 ml) of terbinafine hydrochloride and triamcinolone acetonide, respectively, using their prepared working solutions (40 μg $ml^{-1}$) into 10 ml measuring flasks, dilute to volume with methanol to get final concentrations ranged from 5 to 30 and 4 to 24 μg $ml^{-1}$, respectively. Plot peak amplitudes at 297 and 274 nm, respectively, versus the corresponding concentrations to obtain calibration curve and compute the regression equation.

*2.6.1.2. Assay of laboratory prepared mixtures*. Record the 1st derivative spectrum of laboratory prepared mixtures containing different ratios of terbinafine hydrochloride and triamcinolone acetonide. Measure $D_1$ values at 297 and 274 nm, respectively, then calculate the concentration of terbinafine hydrochloride and triamcinolone acetonide from the corresponding regression equations.

*2.6.1.3. Application to pharmaceutical preparation.* *Lamisil tablets*. Weigh and finely powder not less than 20 tablets. Transfer a portion of powdered tablets equivalent to 10 mg of terbinafine hydrochloride into 10 ml measuring flask shake and dissolve in methanol to obtain a concentration of 1 mg $ml^{-1}$. Transfer 1 ml of extract into 25 ml volumetric flask and dilute to the mark with methanol to get a final concentration of 40 μg $ml^{-1}$, then proceed as under construction of calibration curve starting from 'accurately measured volume [1.25, 2.5–7.5] of terbinafine hydrochloride …'.

*Kenacort tablet*. Weigh and finely powder not less than 20 tablets. Transfer a portion of powdered tablets equivalent to 10 mg of triamcinolone acetonide into 10 ml measuring flask shake and dissolve in methanol to obtain a concentration of 1 mg $ml^{-1}$. Transfer 1 ml of extract into 25 ml volumetric flask and dilute to the mark with methanol to get a final concentration of 40 μg $ml^{-1}$, then proceed as under construction of calibration curve starting from 'accurately measured volume [1, 2–6] of triamcinolone acetonide …'.

*Lamisil cream*. Homogenise the contents of three tubes of the cream. Take a weight of the homogenised cream equivalent to 10 mg of terbinafine hydrochloride into a 10 ml measuring flask. Dissolve in 25 ml methanol and complete to the mark with the same solvent. About 1 ml of this solution is claimed to contain 0.1 mg of terbinafine hydrochloride. Determine the concentration of terbinafine hydrochloride in the above solution.

### *2.6.2. Ratio-spectra 1st derivative ($RSD_1$) spectrophotometric method*

*2.6.2.1. Construction of calibration curve*

*For terbinafine hydrochloride*. The absorption spectra of terbinafine hydrochloride in the range of 5–30 μg $ml^{-1}$ were divided by absorption spectrum of triamcinolone acetonide (24 μg $ml^{-1}$) where the obtained ratio spectra were differentiated with respect to wave length and 1st derivative values at 298 nm were plotted versus the corresponding concentration and the regression equation was computed.

*For triamcinolone acetonide*. The absorption spectra of triamcinolone acetonide in the range of 4–24 μg $ml^{-1}$ were divided by absorption spectrum of terbinafine hydrochloride (30 μg $ml^{-1}$) $RSD_1$ values at 248 nm were recorded, plotted versus the corresponding concentration and the regression equation was computed.

*Assay of laboratory—prepared mixtures*. The absorption spectra of different laboratory-prepared mixtures were divided by absorption spectrum of triamcinolone acetonide (24 μg $ml^{-1}$) for the determination of terbinafine hydrochloride and the absorption spectrum of terbinafine hydrochloride (30 μg $ml^{-1}$) for the determination of triamcinolone acetonide. The $RSD_1$ values were recorded at 298 and 248 nm for terbinafine hydrochloride and triamcinolone acetonide, respectively. The concentration of each one was calculated from the corresponding regression equation.

### *2.6.3. Spectrodensitometric method*

*2.6.3.1. Construction of calibration curves*. Apply separately 2.5–25 μl of the working solution of terbinafine hydrochloride (1 mg $ml^{-1}$) and 2.5–25 μl of triamcinolone acetonide working solution (1 mg $ml^{-1}$) to a thin layer chromatographic plate (20 × 20 cm) using 10 μl Hamilton syringe. Leave a space of 1 cm between each spot and 2 cm from the bottom edge of the plate. Develop the plates in a chromatographic tank previously saturated for at least half an hour with the developing mobile phase, ether:dichloromethane: methanol (5:19.5:0.5 v/v/v) by ascending chromatography at room temperature. Scan the spots of terbinafine hydrochloride and triamcinolone acetonide at 283 and 238 nm, respectively. Construct calibration curves by plotting the area under the peak versus the corresponding concentration, and calculate the corresponding regression equations.

*2.6.3.2. Assay of laboratory—prepared mixtures*. Apply 5 μl of prepared mixtures to silica gel plate as mentioned under construction of calibration curves. Record the area under the peaks at 283 nm for terbinafine hydrochloride and 238 nm for

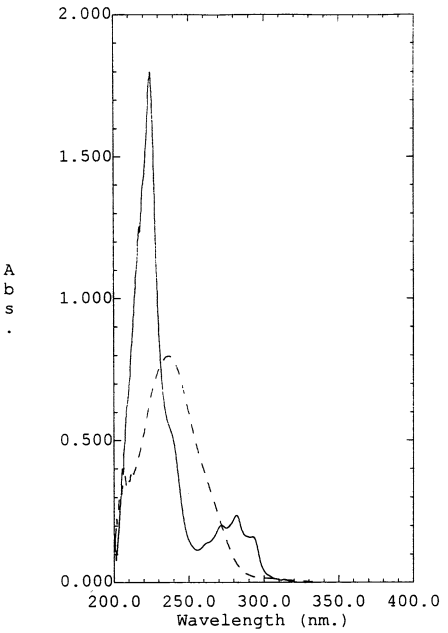


Fig. 2. Absorption spectra of (—), terbinafine hydrochloride (10 μg ml$^{-1}$) in methanol; (- - - -), triamcinolone acetonide (20 μg ml$^{-1}$) in methanol.

triamcinolone acetonide. Calculate the concentration of terbinafine hydrochloride and triamcinolone acetonide from the corresponding regression equations.

*2.6.3.3. Application to pharmaceutical preparations*

*For terbinafine hydrochloride (Lamisil tablets).* Follow the procedure of $D_1$ spectrophotometric method up to 'into 10 ml volumetric flask and completed to the volume with methanol (1 mg ml$^{-1}$) …'. Then follow the procedure detailed under construction of calibration curve for terbinafine hydrochloride by spectrodensitometric method.

*For triamcinolone acetonide (Kenacort tablets).* Proceed as mentioned under the procedure of $RSD_1$ spectrophotometric method up to 'complete to volume with methanol (1 mg ml$^{-1}$) …'. Then follow the procedure detailed under construction of calibration curve for triamcinolone acetonide by spectrodensitometric method.

## 3. Results and discussion

New methods for simultaneous determination of two or more compounds in the same sample, without previous chemical separation, are always of interest. This work is devoted for the analysis of terbinafine hydrochloride alone or in presence of triamcinolone acetonide which are possibly available together in ointment and cream. High performance liquid chromatography was used for simultaneous determination of both drugs [28].

### *3.1. First derivative ($D_1$) spectrophotometric method*

Derivative spectrophotometry offers greater selectivity than does normal spectrophotometry, because it decreases spectral overlap and allows better resolution [29].

Zero order absorption spectra of terbinafine hydrochloride and triamcinolone acetonide showed spectral overlapping (Fig. 2).

First derivative ($D_1$) spectrophotometric technique was used to resolve spectral overlapping of the absorption spectra of terbinafine hydrochloride and triamcinolone acetonide, Fig. 3. By applying $D_1$ technique, zero crossing point for terbinafine hydrochloride with triamcinolone acetonide was shown at 297 nm. A linear correlation was obtained between peak amplitude and the corresponding concentration in the range of 5–30 μg ml$^{-1}$ for terbinafine hydrochloride, from which the linear regression equation was computed and found to be:

$$Y = 0.3129X + 0.0667 \qquad r = 0.9993$$

where $Y$ is peak amplitude at 297 nm, $X$ is the concentration in μg ml$^{-1}$ and $r$ is the correlation coefficient.

The proposed method is valid for determination of terbinafine hydrochloride in presence of triamcinolone acetonide in different laboratory prepared mixtures with mean percentage recoveries of $100.06 \pm 0.57$ as represented in Table 1.

The suggested method has been applied to assay terbinafine hydrochloride in Lamisil tablets and cream, and its validity was further assessed by applying the standard addition technique (Table 2).

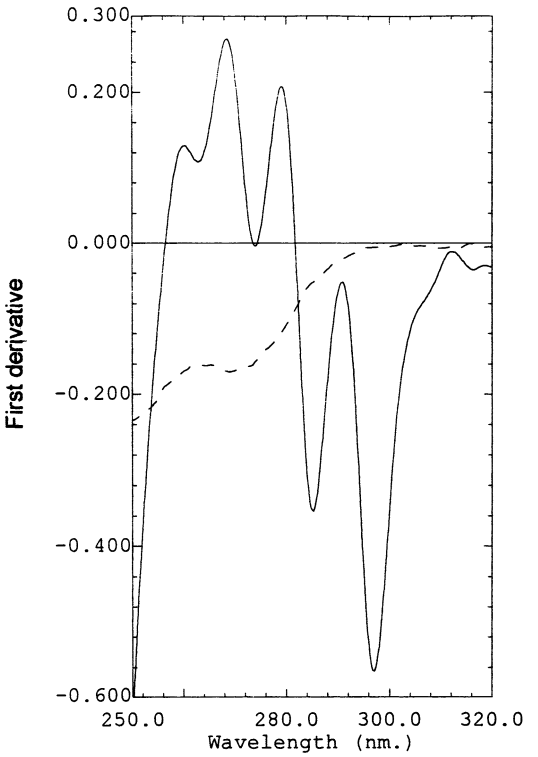


Fig. 3. First derivative absorption spectra of (—), terbinafine hydrochloride (20 μg $ml^{-1}$) in methanol; (----), triamcinolone acetonide (20 μg $ml^{-1}$) in methanol.

Second derivative ($D_2$) spectrophotometric technique can also be used to resolve spectral overlapping of the absorption spectra of terbinafine hydrochloride at 300 nm and triamcinolone acetonide at 278 nm, Fig. 4. However, determination of triamcinolone acetonide was more accurate using ($D_1$) spectrophotometric technique. Direct spectrophotometry (zero order) can also be used for the determination of terbinafine hydrochloride alone at 283 nm. A linear correlation was obtained between the absorbance and the corresponding concentration in the range of 5–40 μg $ml^{-1}$ for terbinafine hydrochloride, from which the linear regression equation was computed and found to be:

$$Y = 0.0234X + 0.0005 \qquad r = 0.9999$$

where $Y$ is absorbance at 283 nm, $X$ is the concentration in μg $ml^{-1}$ and $r$ is the correlation coefficient.

### 3.2. Ratio-spectra 1st derivative ($RSD_1$) spectrophotometric method

Taking in consideration the theory of derivative ratio spectrophotometry [29], we can solve the problem of overlapped absorption spectra of terbinafine hydrochloride and triamcinolone acetonide.

For determination of terbinafine hydrochloride in presence of triamcinolone acetonide, the absorption spectra of different concentrations of terbinafine hydrochloride in the range of 5–30 μg $ml^{-1}$ were divided by the absorption spectrum of triamcinolone acetonide (24 μg $ml^{-1}$). The obtained ratio spectra were differentiated with re-

Table 1
Determination of terbinafine hydrochloride and triamcinolone acetonide in laboratory-prepared mixtures by $D_1$ spectrophotometric method

| Mixture number | Terbinafine hydrochloride | | | Triamcinolone acetonide | | |
|---|---|---|---|---|---|---|
| | Claimed taken (μg $ml^{-1}$) | Found (μg $ml^{-1}$) [a] | Found (%) | Claimed taken (μg $ml^{-1}$) | Found (μg $ml^{-1}$)[a] | Found (%) |
| 1 | 30 | 30.072 | 100.24 | 4 | 4.013 | 100.33 |
| 2 | 25 | 25.030 | 100.12 | 8 | 7.973 | 99.66 |
| 3 | 20 | 20.210 | 101.05 | 12 | 11.946 | 99.55 |
| 4 | 15 | 14.954 | 99.69 | 16 | 16.089 | 100.56 |
| 5 | 10 | 9.880 | 99.88 | 20 | 20.126 | 100.63 |
| 6 | 5 | 4.969 | 99.38 | 24 | 24.219 | 100.91 |
| Mean ± S.D. | | | 100.06 ± 0.57 | | | 100.27 ± 0.55 |

[a] Average of four determinations.

Table 2
Application of standard addition technique to the analysis of terbinafine hydrochloride in Lamisil tablets by $D_1$ method

| Product | Found (%)[a] | Pure added (μg ml$^{-1}$) | Found (μg ml$^{-1}$)[a] | Recovery (%) |
|---|---|---|---|---|
| Lamisil tablet (125 mg) (batch number B004) | 100.91 ± 0.58 | 5 | 5.015 | 100.30 |
| | | 10 | 9.966 | 99.66 |
| | | 15 | 15.105 | 100.70 |
| | | 20 | 19.965 | 99.83 |
| Mean ± S.D. | | | | 100.12 ± 0.47 |
| Lamisil tablet (250 mg) (batch number B013) | 100.29 ± 0.78 | 5 | 4.982 | 99.64 |
| | | 10 | 10.101 | 101.01 |
| | | 15 | 14.985 | 99.90 |
| | | 20 | 20.104 | 100.52 |
| Mean ± S.D. | | | | 100.27 ± 0.62 |
| Lamisil cream (batch number B0064) | 99.35 ± 0.69 | 5 | 5.014 | 100.28 |
| | | 10 | 9.985 | 99.85 |
| | | 15 | 15.025 | 100.17 |
| | | 20 | 20.139 | 100.70 |
| Mean ± S.D. | | | | 100.25 ± 0.27 |
| Kenacort tablet (batch number L92753) | 99.51 ± 0.62 | 4 | 4.003 | 100.08 |
| | | 8 | 7.982 | 99.78 |
| | | 12 | 12.007 | 100.06 |
| | | 16 | 15.994 | 99.96 |
| Mean ± S.D. | | | | 99.97 ± 0.17 |

[a] Average of four determinations.

spect to wavelength, Fig. 5. $RSD_1$ values showed good linearity and accuracy at 298 nm. The linear regression equations were computed and found to be:

$$Y = 0.0793X + 0.0507 \qquad r = 0.9996$$

where $Y$ is $RSD_1$ value at 298 nm, $X$ is the concentration in μg ml$^{-1}$, $r$ is the correlation coefficient.

$RSD_1$ for determination of terbinafine hydrochloride in the presence of triamcinolone acetonide can also be determined at 282 and 290 nm where the $RSD_1$ value showed also good linearity and accuracy but less than at 298 nm.

Determination of triamcinolone acetonide in the presence of terbinafine hydrochloride was achieved by dividing the spectra of different concentrations of triamcinolone acetonide in the range of 4–24 μg ml$^{-1}$ with the spectrum of 30 μg ml$^{-1}$ terbinafine hydrochloride. The obtained ratio spectra were then differentiated with respect to wavelength (Fig. 6). $RSD_1$ values showed good linearity and accuracy at 248 nm. The linear regression equation was computed and found to be.

$$Y = 0.0451X + 0.0132 \qquad r = 0.9998$$

where $Y$ is $RSD_1$ value at 248 nm, $X$ is the concentration in μg ml$^{-1}$ and $r$ is the correlation coefficient.

$RSD_1$ for determination of triamcinolone acetonide in the presence of terbinafine hydrochloride can also be determined at 260 nm where the $RSD_1$ value showed good linearity and accuracy but less than at 248 nm.

Results obtained in Table 3 showed that the proposed method is valid and applicable for determination of terbinafine hydrochloride and triamcinolone acetonide simultaneously in different laboratory prepared mixtures with mean percentage recoveries of 100.22 ± 0.51 and 99.93 ± 0.56, respectively.

The validity of $RSD_1$ spectrophotometric method was further assessed by applying standard addition technique for the analysis of Lamisil tablets (Table 4).

### 3.3. Spectrodensitometric method

Densitometry offers a simple way of quantifying directly on a TLC plate by measuring the optical density of the separated spots. The amounts of compounds are determined by comparing them to a standard curve from reference materials chromatographed simultaneously under the same condition [30].

This method is concerned with the application of spectrodensitometric technique for the determination of terbinafine hydrochloride in presence of triamcinolone acetonide and in their pharmaceutical preparations. The proposed technique is based on the difference of $R_f$ values of terbinafine hydrochloride ($R_f = 0.81$) and triamcinolone acetonide ($R_f = 0.23$).

Different developing systems were tried, but complete separation of the two drugs was achieved using ether: dichloromethane: methanol (5:19.5:0.5 v/v/v). The separated spots of each of terbinafine hydrochloride and triamcinolone acetonide can be scanned on the same plate at 283 and 238 nm, respectively. A linear correlation was

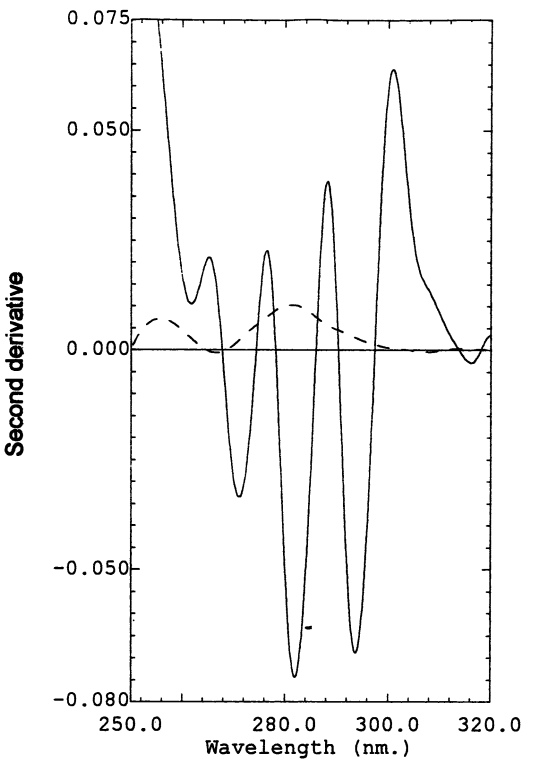


Fig. 4. Second derivative absorption spectra of (—), terbinafine hydrochloride (10 μg ml$^{-1}$) in methanol; (- - - -), triamcinolone acetonide (10 μg ml$^{-1}$) in methanol.

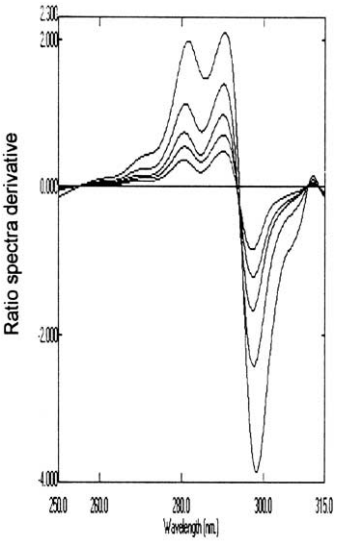


Fig. 5. Calibration curve of radio-spectra 1st derivative of 5–30 μg ml$^{-1}$ of terbinafine hydrochloride/24 μg ml$^{-1}$ triamcinolone acetonide.

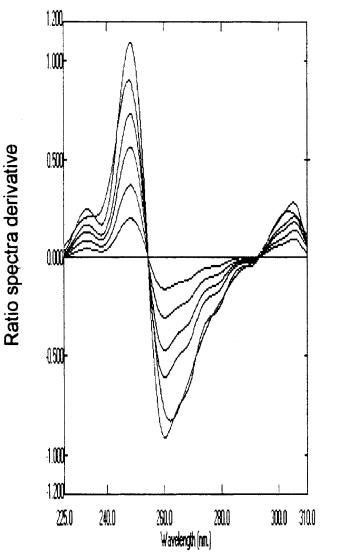


Fig. 6. Calibration curve of radio-spectra 1st derivative of 4–24 μg ml$^{-1}$ of terbinafine hydrochloride/30 μg ml$^{-1}$ triamcinolone acetonide.

obtained between peak area and concentration in the range of 5–25 μg spot$^{-1}$ for terbinafine hydrochloride and 2.5–22.5 μg spot$^{-1}$ for triamcinolone acetonide. The linear regression equations were computed and found to be:

$$Y = 0.5708X + 1.265 \qquad r = 0.9987$$

$$Y = 0.5476X + 2.0167 \qquad r = 0.09986$$

For terbinafine hydrochloride and triamcinolone acetonide, respectively, where $Y$ is the area under the peak, $X$ is the concentration in μg spot$^{-1}$ and $r$ is the correlation coefficient.

Results obtained by applying spectrodensitometric procedure showed that the concentration of terbinafine hydrochloride and triamcinolone acetonide can be simultaneously determined in the prepared mixtures with mean percentage accuracy of $99.77 \pm 0.74$ and $100.07 \pm 0.78$, respectively (Table 5).

Table 3
Determination of terbinafine hydrochloride and triamcinolone acetonide in laboratory-prepared mixtures by $RSD_1$ spectrophotometric method

| Mixture number | Terbinafine hydrochloride | | | Triamcinolone acetonide | | |
|---|---|---|---|---|---|---|
| | Claimed taken (μg ml$^{-1}$) | Found (μg ml$^{-1}$)[a] | Found (%) | Claimed taken (μg ml$^{-1}$) | Found (μg ml$^{-1}$)[a] | Found (%) |
| 1 | 30 | 30.230 | 100.77 | 4 | 3.983 | 99.58 |
| 2 | 25 | 24.891 | 99.56 | 8 | 7.991 | 99.89 |
| 3 | 20 | 19.971 | 99.86 | 12 | 11.896 | 99.13 |
| 4 | 15 | 15.009 | 100.06 | 16 | 15.986 | 99.91 |
| 5 | 10 | 10.084 | 100.84 | 20 | 20.110 | 100.55 |
| 6 | 5 | 5.012 | 100.24 | 24 | 24.125 | 100.52 |
| Mean ± S.D. | | | 100.22 ± 0.51 | | | 99.93 ± 0.56 |

[a] Average of four determinations.

Table 4
Application of standard addition technique to the analysis of terbinafine hydrochloride and triamcinolone acetonide in pharmaceutical preparations by $RSD_1$ spectrophotometric method

| Product | Found (%)[a] | Pure added (μg ml$^{-1}$) | Found (μg ml$^{-1}$)[a] | Recovery (%) |
|---|---|---|---|---|
| Lamisil tablet (125 mg) (batch number B004) | 100.42 ± 0.465 | 5 | 5.025 | 100.50 |
| | | 10 | 9.960 | 99.60 |
| | | 15 | 15.165 | 101.10 |
| Mean ± S.D. | | | | 100.40 ± 0.75 |
| Lamisil tablet (250 mg) (batch number B013) | 100.63 ± 0.718 | 5 | 5.000 | 100.00 |
| | | 10 | 10.130 | 101.30 |
| | | 15 | 14.895 | 99.30 |
| Mean ± S.D. | | | | 100.20 ± 1.01 |
| Lamisil cream (batch number B0064) | 99.25 ± 0.835 | 5 | 5.026 | 100.52 |
| | | 10 | 9.885 | 98.85 |
| | | 15 | 14.925 | 99.50 |
| Mean ± S.D. | | | | 99.62 ± 0.84 |
| Kenacort tablet (batch number L92753) | 100.50 ± 0.286 | 5 | 4.963 | 99.26 |
| | | 10 | 9.932 | 99.32 |
| | | 15 | 15.000 | 100.00 |
| Mean ± S.D. | | | | 99.53 ± 0.41 |

[a] Average of four determinations.

Table 5
Determination of terbinafine hydrochloride and triamcinolone acetonide in laboratory-prepared mixtures by spectrodensitometric method

| Mixture number | Terbinafine hydrochloride | | | Triamcinolone acetonide | | |
|---|---|---|---|---|---|---|
| | Claimed taken ($\mu g\ ml^{-1}$) | Found ($\mu g\ ml^{-1}$)[a] | Found (%) | Claimed taken ($\mu g\ ml^{-1}$) | Found ($\mu g\ ml^{-1}$)[a] | Found (%) |
| 1 | 9 | 8.982 | 99.80 | 1 | 0.996 | 99.60 |
| 2 | 7 | 7.001 | 100.01 | 3 | 3.024 | 100.80 |
| 3 | 5 | 4.925 | 98.50 | 5 | 4.956 | 99.12 |
| 4 | 3 | 3.011 | 100.37 | 7 | 7.065 | 100.93 |
| 5 | 2 | 2.003 | 100.15 | 8 | 7.990 | 99.88 |
| Mean ± S.D. | | | 99.77 ± 0.74 | | | 100.07 ± 0.78 |

[a] Average of four determinations.

Table 6
Application of standard addition technique to the analysis of terbinafine hydrochloride and triamcinolone acetonide in pharmaceutical preparations by spectrodensitometric method

| Product | Found (%)[a] | Pure added ($\mu g\ spot^{-1}$) | Pure found ($\mu g\ spot^{-1}$)[a] | Recovery (%) |
|---|---|---|---|---|
| Lamisil tablet (125 mg) (batch number B004) | 99.48 ± 0.66 | 5 | 4.950 | 99.00 |
| | | 7.5 | 7.558 | 100.77 |
| | | 10 | 10.106 | 101.06 |
| | | 12.5 | 12.618 | 100.94 |
| Mean ± S.D. | | | | 100.44 ± 0.97 |
| Lamisil tablet (250 mg) (batch number B013) | 100.67 ± 0.37 | 5 | 5.012 | 100.50 |
| | | 7.5 | 7.525 | 99.85 |
| | | 10 | 10.126 | 101.26 |
| | | 12.5 | 12.548 | 100.38 |
| Mean ± S.D. | | | | 100.55 ± 0.48 |
| Lamisil cream (batch number B064) | 100.92 ± 0.76 | 5 | 4.956 | 99.12 |
| | | 7.5 | 7.583 | 101.11 |
| | | 10 | 10.087 | 100.87 |
| | | 12.5 | 12.613 | 100.90 |
| Mean ± S.D. | | | | 100.50 ± 0.93 |
| Kenacort tablet (batch number L92753) | 99.45 ± 0.47 | 4 | 4.004 | 100.10 |
| | | 8 | 8.012 | 100.15 |
| | | 12 | 12.039 | 100.33 |
| | | 16 | 15.888 | 99.30 |
| Mean ± S.D. | | | | 99.97 ± 0.51 |

[a] Average of four determinations.

The proposed method has been applied to assay terbinafine hydrochloride in Lamisil tablets and triamcinolone acetonide in Kenacort tablets. The validity of the suggested procedures was further assessed by applying the standard addition technique (Table 6).

Statistical comparison of the results obtained by the proposed and reference methods [13,26] for pure drugs separately were showed in Table 7. No significant difference between the proposed methods and reference methods was found with respect to precision and accuracy.

Table 7
Statistical analysis of the results obtained by applying the proposed and reference methods [13,26] for the analysis of pure samples of terbinafine hydrochloride and triamcinolone acetonide

| Values | The proposed methods | | | | | | Reference methods [13,26] | |
|---|---|---|---|---|---|---|---|---|
| | First derivative $D_1$ method | | Ratio-spectra 1st derivative ($RSD_1$) method | | Spectrodensitometric method | | | |
| | Terbinafine hydrochloride | Triamcinolone acetonide | Terbinafine hydrochloride | Triamcinolone acetonide | Terbinafine hydrochloride | Triamcinolone acetonide | Terbinafine hydrochloride | Triamcinolone acetonide |
| Mean ± S.D. | 100.06 ± 0.57 | 100.27 ± 0.55 | 100.22 ± 0.51 | 99.93 ± 0.56 | 99.77 ± 0.74 | 100.07 ± 0.78 | 99.88 ± 0.65 | 100.49 ± 0.45 |
| *N* | 6 | 6 | 6 | 6 | 6 | 6 | 4 | 4 |
| Variance | 0.325 | 0.303 | 0.260 | 0.314 | 0.548 | 0.608 | 0.423 | 0.203 |
| *t* (2.306)[a] | 0.450 | 0.692 | 0.881 | 1.746 | 0.248 | 1.077 | – | – |
| *F* (9.01)[a] | 1.302 | 1.493 | 1.627 | 1.547 | 1.296 | 2.995 | – | – |

[a] The values in parenthesis are corresponding to the theoretical values of $t$ and $F$ at ($P = 0.05$).

The results obtained by applying the proposed procedures suggested that, they could be applied for the simultaneous determination of terbinafine hydrochloride and triamcinolone acetonide. Moreover, the methods are rapid, sensitive, selective and could be safely used in routine and quality control analysis.

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