FTIR Spectrometric Determination of Sulphamethoxazole and Trimethoprim in Co-Trimoxazole Tablets

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A method has been developed for the determination of sulphamethoxazole (SMX) and trimethoprim (TMP) in pharmaceuticals by fourier transform infrared (FTIR) spectrometry. The method is based on the fractional dissolving of SMX and TMP in acetone and chloroform respectively. SMX is then determined by absorbance measurements at 1165 cm^{-1} and TMP by using the absorbance values at 1126 cm^{-1}, separately. The method provides precise and accurate results for the analysis of real samples of the binary dosage form of SMX and TMP, co-trimoxazole.

Sulphamethoxazole and trimethoprim are substances often found associated in pharmaceutical dosage forms used as antibacterial. Therefore, the determination of the two drugs is a frequent analytical problem in quality control of the pharmaceutical industry. Both TMP and SMX, have been measured in binary mixtures by non-aqueous titrimetry[1], densitometry[2], potentiometry[3], colorimetry[4], TLC[5], HPLC[6] and spectrophotometry[7-9]. FTIR spectrometry has been also used for simultaneous determination of SMX and TMP[10-12]. These FTIR spectrometric methods have complicated procedures and/or suffer from expensive reflectance accesories. In the present study, a rapid and reliable method based on IR spectrometry for simultaneous determination of SMX and TMP is described in a well known pharmaceutical formulation, co-trimoxazole.

Commercial samples of co-trimoxazole were obtained from a local pharmacy. Analytical grade SMX and TMP were obtained from Sobhan Co. (Tehran, Iran). All other chemicals and solvents were of analytical-reagent grade. Spectrometric determinations were performed using a Nicolet magna 750 FTIR spectrometer (Madison, USA) equipped with a Ge/KBR splitter and a DTGS detector. All the measurements were carried out using a micro flow ceil from Spectra Tech (Stamford, USA) with ZnSe windows and 0.1 mm PTFE spacer.

Accurately weighed amounts of SMX and TMP were respectively dissolved in 25 ml of acetone and 10 ml chloroform. The spectrum was recorded for each standard solution at a resolution of 4 cm^{-1} with 32 coadded scans by considering the solvent as reference. Five authentic mixtures of TMP, SMX and starch (as excipient) were prepared as real samples. Composition of the standards is summarized at Table 1. An accurately weighed quantity of the homogenized powdered samples containing 100-400 mg of SMX and 20-120 mg of TMP was placed in a 20 ml glass tube and 10 ml of acetone was added. The tube was shaken mechanically for 5 min and centrifuged for 3 min. The supernatant was decanted in a 25 ml graduated flask. The leaching procedure for SMX was followed three more times with 4 ml of acetone. The collected leaching solution was diluted to volume to volume with acetone. TMP was leached from the residual material with chloroform in three stages (5 ml/2ml/2ml). The solution diluted finally to a 10 ml volume.

Fig. 1. shows the FTIR spectra of standard solutions of SMX (in acetone) and TMP (in chloroform) in the range of 1200-1100 cm^{-1}. As shown in this figure, intensity of spectral bands are obviously linear with concentrations of the compounds. The FTIR absorbance spectra of SMX and TMP, obtained in the solution, present well defined and intense bands in this range. The band of SMX at 1162 cm^{-1} is the most sensitive and obeys Beers law, consequently it seems the most appropriate for the SMX determination. The 1126 cm^{-1} band represents the best

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Table 1 - Analysis of standard samples

Sample	Actual composition SMX, mg	TMP, mg	Results obtained (Relative error%) starch, mg	SMX, mg	TMP, mg
1	400	80	50	389(-2.75)	75(-6.25)
2	200	100	50	196(-2.00)	97(-3.00)
3	300	100	75	296(-1.33)	96(-4.00)
4	400	80	100	391(-2.25)	76(-5.00)
5	500	80	100	488(-2.40)	77(-3.75)

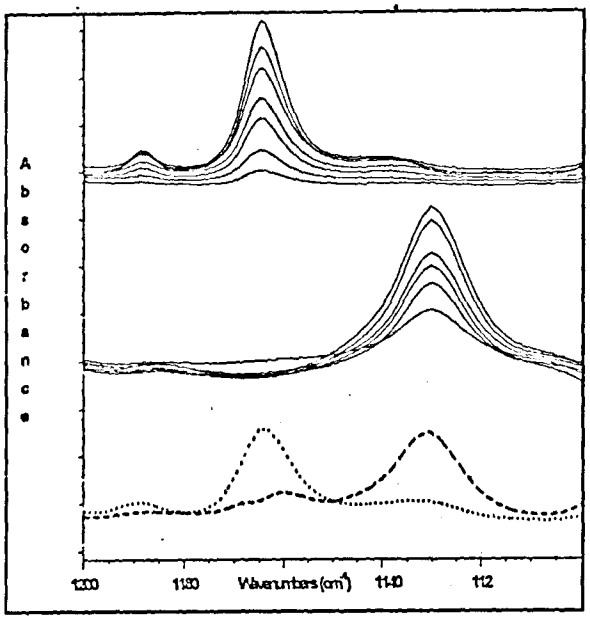

Fig. 1 : IR difference spectra of SMX standard solutions (top), TMP standard solutions (middle) and leached solutions of SMX (..) and TMP (- -) from commercial drug powder (bottom)

potential wavenumber for the determination of TMP, due to its high sensitivity. The solvents leach the drugs selectively but do not dissolve the excipients, therefore, no other considerable spectral interferences are expected.

Table 2 - Figures of merit of FTIR determination of SMX (in acetone solutions) and TMP in chloroform solutions)

Parameter	SMX	TMP
Dynamic Range (mg/ml)	0-20	0-16
Sensitivity (au.ml/mm/mg)	0.297	0.212
Limit of Detection (μg/ml)	44	35
Repeatability, RSD%, n*=5	0.12%	0.19%
Precision, RDS%, n**=5	2.4%	2.8%

n*=5 measurements of two sample solutions containing 12 mg/ml SMX and 6mg/ml TMP, respectively.
n**=5 independent analysis of the same standard solid mixture containing 300 mg SMX and 60 mg TMP.

The FTIR determination of SMX and TMP had been established from the characteristics of the analytical lines and also from a series of analysis carried out at different concentration levels. Analytical results for standard sam-

Table 3 - Analysis of commercial samples by FTIR spectrometry

Pharmaceutical/Manufacturer	SMX Theo.	TMP Theo.	SMX FTIR	TMP FTIR	SMX BP	TMP BP
Cotrimoxazole/Chemidarou	400	80	383	76.7	385	75.5
Cotrimoxazole/Chemidarou	100	20	96	20.4	96	19.5
Cotrimoxazole/Alborzdarou	400	80	383	77	392	76

Theo.= Theoretical content (mg per tablet) FTIR = FTIR results (mg per tablet)
BP = Results according to British Pharmacopoeia (mg per tablet)

ples are given in Table 1. Table 2 summarizes the values found for the analytical parameters obtained for each compound considered. Three Iranian commercial co-trimoxazole tablets were analyzed by using two methods, the FTIR method and BP standard method[13]. Results obtained are summarized in Table 3. These results show good agreements between there two methods.

The results obtained show that the developed procedure gives levels of accuracy and precision comparable to those obtained by BP standard method. Therefore, this approach could be considered as a good alternative for the simultaneous determination of active principles in the quality control of this type of pharmaceutical.

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Phytochemical Investigation of *Parkinsonia aculeata*

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***Parkinsonia aculeata* stems have been shown to contain glycerol β-butanoate α, α'-dipentanoate, β-sitosterol, glycerol α-heptanoate ∝'octanoate, β-sitosteryl-β-D-glucoside and sucrose. Of these, the two glycerides are being reported for the first time.**

Parkinsonia aculeata belongs to Leguminosae family and *Caesalpiniaceae* subfamily. Its flowers have been reported[1] to have antipyretic activity. Its alcoholic extract exhibits central nervous system depressant activity and its aqueous extract shows cholinomimetic activity[2]. A literature survey reveals that there is no report on the chemical investigation of its stems. The present work has therefore been carried out to isolate and characterise the chemical components of its stems.

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The ^1H NMR was recorded on Bruker AC-300F 300MHz NMR spectrometer in $CDCl_3$ using TMS as the internal standard. The other instruments used are Hitachi 570 infrared spectrophotometer and VG-70S 11-250J GCMS-DS Mass Spectrometer.

Stems of *P. aculeata* (5 kg) were collected from the Landscape, CCSHAU, Hisar. These were chopped into small pieces and extracted with hot methanol. Extractives were subjected to silica gel column chromatography. Elutions have afforded five compounds. These are (i) glycerol β-butanoate α,α'-dipentanoate (**1**, 10 mg), (ii) β-sito-