The results obtained show that the amounts of propyphenazone and ketoprofen contained in the formulations conform to the specifications of the B.P.\(^3\) (Table I). Since an official method of analysis is not available for the simultaneous determination of the present drug combination, the proposed HPLC method is precise, accurate and reproducible. This is evidenced by their separation, quantitation and standard deviations obtained in our experiments. The proposed method thus should become very valuable in the analysis of the present combination preparations.

ACKNOWLEDGEMENTS

The authors wish to thank M/s Plethico Pharmaceuticals Ltd., Indore and Juggat Pharmaceuticals Ltd., Bangalore for the supply of pure drug samples.

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Simultaneous Spectrophotometric Determination of Rifampicin, Isoniazid and Pyrazinamide in Combined Pharmaceutical Dosage Forms

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A simple spectrophotometric method requiring no prior separation has been developed for the simultaneous determination of Rifampicin, Isoniazid and Pyrazinamide in combination in pharmaceutical formulations. The method described in precise, accurate, reproducible and rapid.

RIFAMPICIN (RIF), Isoniazid (INH) and Pyrazinamide (PYZ) are effective drugs for the treatment of tuberculosis. The drugs are used either in single or combination formulations which forms the first line treatment for tuberculosis. Fixed combination of RIF (150 mg), INH (100 mg) and PYZ (350 mg) are being marketed as tablet.

* For correspondence
The official assay methods are available for analysis of individual drugs and their formulations listed in IP\(^1\) and USP\(^2\). The other methods available in literature are ion pair extraction,\(^3\) HPTLC,\(^4\) Titrimetry\(^5\) for RIF, HPLC\(^6\), Colorimetric,\(^7\) Oscilopolarography\(^8\) for INH and Polarography,\(^9\) Spectrophotometric,\(^10\) HPLC\(^11\) for PYZ. The correlation between slope (1), Intercept (i), and coefficient of correlation (r) was evaluated by means of the least squares method. The result obtained by replicate determination are given in Table 1.

Aliquots of 7.5 ml of RIF, 5.0 ml of INH and 17.5 ml of PYZ stock solution were mixed in a 100 ml volumetric flask followed by dilution to mark with water.

From the aliquotes of standard solution, four mixed standards were prepared having ratio and of RIF, INH, PYZ (1.5 : 1.0 : 3.5; 4.5 : 3.0 : 10.5; 9.0 : 6.0 : 21.0; and 12.0 : 8.0 : 28.0 µg/ml). These were scanned over the range of 350-200 nm in the multicomponent mode. The overlay spectrum for these four mixed standards were obtained and used later to determine the concentration of RIF, INH and PYZ in their sample solution fig. 1.

For tablet formulation, twenty tablets were weighed and ground into a fine powder. An accurately weighed powder sample equivalent to 9.0 mg of RIF, 6.0 mg of INH and 21.0 mg of PYZ was transferred to a 100 ml volumetric flask and was dissolved in 5.0 ml of distilled water. The solution was allowed to stand for 15 minute with frequent shaking and finally diluted to volume with distilled water, filtered and diluted (16.6 ml filtrate to 100 ml with distilled water). Two milliliter, 3.0 ml, 4.0 ml, 5.0 ml and 6.0 ml aliquotes of above solution were pipetted out separately in a 10 ml calibrated flask and were finally diluted to volume with distilled water.

In order to assess the validity of the proposed method for assaying each drug in presence of other component, different concentration of each drug were prepared and assayed using the multicomponent determination procedure. Results are presented for RIF, INH and PYZ in Table 2.

Concentration of each component (RIF, INH and PYZ) of the sample solution was obtained from calibration curve precalibrated from measured mixed...
Table 1: Result of Linearity Test (n=7)

<table>
<thead>
<tr>
<th>Analyte</th>
<th>Regression Parameters</th>
<th>Coefficient of correlation</th>
<th>RSD* %</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Slope (1)</td>
<td>Intercept (i)</td>
<td>(r)</td>
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<tr>
<td>RIF</td>
<td>0.03563</td>
<td>-0.0364</td>
<td>0.9999</td>
</tr>
<tr>
<td>INH</td>
<td>0.029</td>
<td>-0.0012</td>
<td>1.0000</td>
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<tr>
<td>PYZ</td>
<td>0.0597</td>
<td>0.0477</td>
<td>0.9994</td>
</tr>
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</table>

* n = 3
RSD - Relative Standard Deviation

Table 2: Results obtained from authentic and commercial samples

<table>
<thead>
<tr>
<th>Analyte</th>
<th>Authentic Sample</th>
<th>Commercial Sample</th>
<th>Commercial Sample</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Taken µg/ml</td>
<td>Found µg/ml</td>
<td>Relative Error (%)</td>
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<tr>
<td>RIF</td>
<td>3.0</td>
<td>2.96</td>
<td>-0.013</td>
</tr>
<tr>
<td></td>
<td>4.5</td>
<td>4.96</td>
<td>-0.010</td>
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<tr>
<td></td>
<td>6.0</td>
<td>5.92</td>
<td>-0.013</td>
</tr>
<tr>
<td></td>
<td>7.5</td>
<td>7.34</td>
<td>-0.020</td>
</tr>
<tr>
<td></td>
<td>9.0</td>
<td>9.00</td>
<td>0.000</td>
</tr>
<tr>
<td>INH</td>
<td>2.0</td>
<td>1.97</td>
<td>-0.015</td>
</tr>
<tr>
<td></td>
<td>3.0</td>
<td>2.99</td>
<td>-0.003</td>
</tr>
<tr>
<td></td>
<td>4.0</td>
<td>3.94</td>
<td>-0.015</td>
</tr>
<tr>
<td></td>
<td>5.0</td>
<td>4.90</td>
<td>-0.020</td>
</tr>
<tr>
<td></td>
<td>6.0</td>
<td>6.00</td>
<td>-0.000</td>
</tr>
<tr>
<td>PYZ</td>
<td>7.0</td>
<td>6.90</td>
<td>-0.140</td>
</tr>
<tr>
<td></td>
<td>10.5</td>
<td>10.48</td>
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<td>14.0</td>
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<td>17.5</td>
<td>17.13</td>
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<tr>
<td></td>
<td>21.0</td>
<td>21.01</td>
<td>0.010</td>
</tr>
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</table>

RSD = Relative Standard deviation (*n = 5), Relative error (* n = 3), A = Tablet Sample, B = Tablet recovery.
R' = Mean Percent Recovered.

absorption characteristic according to the multicomponent determination procedure. The results obtained by replicate determination following above procedure were shown in Table 2.
Fig. 1: U.V. Spectra of Mixed Standards of RIF, INH and PYZ

To study the recovery of RIF, INH and PYZ, a fixed quantity of a preanalysed sample was taken and estimated by the proposed method. The amount of RIF, INH and PYZ found are recorded in Table 2.

From the recovery of pure drug, tablet sample and tablet recovery, the means were calculated for four degrees of freedom. As $t(0.05,4) = 2.78$, the results of the test shows that recoveries obtained do not differ significantly from 0-100 percent (Table 2). The average recoveries obtained in each instance were compared with the theoretical value of 100 percent by means of student's "t" test. As $t(0.05,4) = 2.78$, it is concluded that the recoveries obtained were in agreement from 100 percent for either drug (Table 2).

The proposed method is simple and convenient for routine simultaneous determination of RIF, INH and PYZ in pharmaceutical formulations. Accuracy of the proposed method was also validated by recovery studies and was found to be 96.67 ± 1.1 for RIF, 96.07 ± 0.89 for INH and 96.22 ± 1.05 for PYZ. Therefore, there was no interference from common adjuvants used in the formulation. The ratio of RIF, INH and PYZ in mixed standard preparation was established after several trials. The values of RSD 0.75 to 1.97 percent are also indicative of accuracy and reproducibility of the proposed method and these merits, in addition to the simple reagent suggest its routine use.

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Preformulation Stability and Permeation Studies of Transdermal Patches of Salbutamol

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Stability and skin permeation of salbutamol base from adhesive matric transdermal patches containing antioxidants and skin permeation enhancers was studied. Skin permeation was enhanced with increase in salbutamol content and oleic acid content in the patches. Accelerated stability testing indicated that patches containing butylated hydroxy toluene and thiourea had an adequate stability profile.

OR chronic management or prophylactic therapy of asthma particularly nocturnal asthma, long acting formulations particularly transdermal delivery would be of benefit. In comparison to oral delivery which has the disadvantage of variable and limited period of residence at the site of absorption as well as potential for dose-dumping, the transdermal route provides more reliable and reproducible delivery. Recent advances in skin permeation enhancement suggest a potentially wider scope in terms of number and types of drugs deliverable by transdermal route.  

0.5 ml of the formulations containing 10 mg/ml of salbutamol (SL), 40 mg/ml of pressure sensitive adhesive (psa) and other ingredients as given in Table I were poured on a 5 sq.cm. area on a backing membrane and allowed to dry in air. The patches were packed in sealed pouches prepared from Scophpak(R) film and stored at 45° (15 days) and 55° (10 days, 20 days). Preliminary compatibility evaluations were carried out by extracting the drug

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