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(2a₁·e₁, a₂·d₂, a₃·d₃, b₄·e₄). The latter on reacting with substituted benzaldehydes in anhydrous sodium acetate afforded 2-phenyl(substituted)-3-aryl-5-benzilidine(substituted)thiazolidine-4-ones (3a₁-e₁, a₂, d₂, a₃, c₃, d₃, b₄·e₄), which in turn reacted with phenylhydrazine in presence of anhydrous sodium acetate to furnish 2-phenyl-3,5-diphenyl(substituted)-6-aryl-3,3a,5,6-tetrahydro-2H-pyrazolo[3,4-d] thiazoles (4a₁-e₁, a₂, d₂, a₃, c₃, d₃, b₄-e₄).

All compounds were screened for their in vitro antibacterial activity by agar cup plate method at 100 μg concentration. Solutions of the test compounds were kept in dimethylsulphoxide. Ampicillin trihydrate (100 μg/ml) was used as a standard drug for comparison and solvent control was kept. The antibacterial activity of various compounds against pathogenic strains in nutrient agar is shown in Table 5. Compounds 4d₁, d₂, d₃, c₄, and d₄ were found to be the most active against all the microbes. However, all the compounds were comparatively less active than the standard drug.

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**REFERENCES**


**TABLE 5: ANTIBACTERIAL ACTIVITIES OF 2-PHENYL-3,5-DIPHENYL(SUBSTITUTED)-6-ARYL-3,3A,5,6-TETRAHYDRO-2H-PYRAZOLO [3,4-D] THIAZOLES**

<table>
<thead>
<tr>
<th>Compound</th>
<th>Inhibition zone diameter (mm)*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>S. a</td>
</tr>
<tr>
<td>4a₁</td>
<td>18</td>
</tr>
<tr>
<td>b₁</td>
<td>19</td>
</tr>
<tr>
<td>c₁</td>
<td>17</td>
</tr>
<tr>
<td>d₁</td>
<td>19</td>
</tr>
<tr>
<td>e₁</td>
<td>17</td>
</tr>
<tr>
<td>a₂</td>
<td>19</td>
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<td>d₂</td>
<td>21</td>
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<tr>
<td>a₃</td>
<td>19</td>
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<td>c₃</td>
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<td>21</td>
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<td>c₄</td>
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<tr>
<td>d₄</td>
<td>20</td>
</tr>
<tr>
<td>e₄</td>
<td>18</td>
</tr>
<tr>
<td>Ampicillin trihydrate</td>
<td>31</td>
</tr>
</tbody>
</table>

*Average of three readings. S. a is Staphylococcus aureus, A. P is Actinomyces pyogenes, K. A is Klebsiella aerogenes and E. c is Escherichia coli

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**Simultaneous Estimation of Aceclofenac, Paracetamol and Chlorzoxazone in Tablets**

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The combination of aceclofenac, paracetamol and chlorzoxazone is emerging as one of the widely prescribed combination in single dosage form. Aceclofenac is a typical Cox-2 inhibitor in combination with muscle relaxant chlorzoxazone and a traditional antipyretic drug paracetamol. Literature revealed that there is no single method for the simultaneous estimation of all these drugs in tablet dosage forms, which prompted us to develop a simple, rapid, accurate, economical and sensitive spectrophotometric method. The simultaneous estimation method is based on the additivity of absorbances, for the determination of aceclofenac, paracetamol and chlorzoxazone in
Aceclofenac is 2[(2,6-dichlorophenyl)amino]benzoic acid carboxymethyl ester is an analgesic and non-steroidal antiinflammatory drug; paracetamol (4-hydroxy acetanilide) is used as an analgesic and anti pyretic drug and chlorzoxazone is 5-chloro-2-benzoxazolol is a commonly prescribed muscle relaxant. Aceclofenac is official in BP1, paracetamol in BP and IP2,3 and chlorzoxazone in USP4. BP suggests a potentiometric assay method for aceclofenac in bulk drugs. The IP and BP both suggest titrimetric and UV spectrophotometric assay method for paracetamol in bulk and tablet formulations. Literature survey revealed that HPLC5, densitometric6, spectrofluorimetric7 and colorimetric8 methods have been reported for the estimation of aceclofenac in pharmaceutical dosage forms. With the advancement in the field of analytical chemistry and software technology different methods have been developed for simultaneous estimation of combination dosage forms. Though the combination is widely prescribed, no simultaneous method is reported for the estimation of the drugs in combined dosage forms. This prompted us to develop simple, rapid, accurate, economical and sensitive spectrophotometric simultaneous method.

The Shimadzu Pharmaspec 1700 UV/Vis spectrophotometer with 10 mm matched quartz cells was used for experiments. The chemicals used were of analytical grade. The commercially available tablets of aceclofenac, paracetamol and chlorzoxazone in combination were procured from local market. Aceclofenac, received as gift sample from Aristo Pharma Ltd., paracetamol (BDH) and chlorzoxazone from Mankind Pharma were used as such without further purification.

Standard stock solution of aceclofenac, paracetamol and chlorzoxazone were prepared separately by dissolving 100 mg each (accurately weighed) of standard aceclofenac, paracetamol and chlorzoxazone in methanol and made up the volume up to 100 ml with same solvent. Working standard solutions (10 µg/ml) (A), (B) and (C) were further prepared by taking 1 ml of stock solution of each drug solution in 100 ml volumetric flasks separately and made up the volume up to the mark with methanol.

Overlain spectra of standard solutions of aceclofenac, paracetamol and chlorzoxazone were scanned (fig. 1). Aceclofenac shows absorption maxima at 276 nm, paracetamol shows at 248 nm and chlorzoxazone at 282 nm. The calibration curves for each were prepared in the concentration range of 2-20 µg/ml at each wavelength i.e. 276 nm, 248 nm and 282 nm. The absorptivity coefficients were determined for all the drugs at all the wavelengths and following equations were made. $A_1 = 306.64\, C_x + 163.16\, C_y + 251.4\, C_z$, $A_2 = 109.52\, C_x + 908.22\, C_y$, $A_3 = 293.77\, C_x + 135.58\, C_y + 325.52\, C_z$, where $A_1, A_2$ and $A_3$ are absorbances at 276 nm, 248 nm and 282 nm, respectively and $C_x, C_y$ and $C_z$ are concentrations of aceclofenac, paracetamol and chlorzoxazone respectively.

Tablet estimation was done on of two brands, Dolokind-MR (Mankind Pharma, Delhi) and Morcket-MR (Moraceae Lab, Luknow). Twenty tablets were weighed and crushed to a fine powder. Powder equivalent to 65 mg of paracetamol, 20 mg of aceclofenac and 50 mg chlorzoxazone (tablet contains 325 mg paracetamol, 100 mg aceclofenac and 250 mg chlorzoxazone) was extracted quantitatively with (4×20) ml of methanol and volume was made up to 100 ml. Insoluble excipients were separated by filtration. The filtrate was further diluted to get final concentration of both the drugs in the linearity range.
Absorbance was noted at the selected wavelengths and concentrations were determined by using the Eqns. 1, 2 and 3.

The method was found to be accurate, simple and rapid, for routine simultaneous analysis of the formulations without prior separation. The content of the aceclofenac, paracetamol and chlorzoxazone was directly found from the Eqns. 1, 2 and 3 using matrices (Cramer’s rule).

\[
\begin{vmatrix}
a_1 & b_1 & c_1 & d_1 \\
a_2 & b_2 & c_2 & d_2 \\
a_3 & b_3 & c_3 & d_3 \\
\end{vmatrix} = D_x, \\
\begin{vmatrix}
a_1 & b_1 & c_1 & d_1 \\
a_2 & b_2 & c_2 & d_2 \\
a_3 & b_3 & c_3 & d_3 \\
\end{vmatrix} = D_y, \\
\begin{vmatrix}
a_1 & b_1 & c_1 & d_1 \\
a_2 & b_2 & c_2 & d_2 \\
a_3 & b_3 & c_3 & d_3 \\
\end{vmatrix} = D_z.
\]

Similarly using the same approach the other determinant Dy and Dz can also be found out.

The reproducibility, repeatability and accuracy of the proposed method were found to be satisfactory which is evidenced by low values of standard deviation, percent relative standard deviation and standard error (Table 1). The percent range of error (within 95% confidence limits) showed precision of the method. The accuracy and reproducibility of the proposed method was confirmed by recovery experiments, performed by adding known amount of the drugs to the pre analyzed formulations and reanalyzing the mixture by proposed method (Table 2). The percent recovery obtained indicates non-interference from the excipients used in the formulations. Thus the method developed in the present investigation found to be simple, sensitive, accurate and precise and can be successfully applied for the simultaneous estimation of aceclofenac, paracetamol and chlorzoxazone in tablets.

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