Abstract:

A large number of organic solvents, viz. acetone, dichloromethane, chloroform, ether, ethyl acetate, ethanol, toluene, hexane, butanol, xylene, heptane and cyclohexane have been employed to perform thin layer chromatography (TLC) of various drugs. Most of these organic solvents are costlier and toxic. To some extent, such solvents are responsible for environmental pollution also.

In the present investigation, hydrotropic solutions were employed as mobile phase to perform TLC of poorly water-soluble drugs precluding the use of organic solvents. Atenolol, paracetamol, ibuprofen, diclofenac sodium & caffeine were selected as model poorly water-soluble drugs; and urea & sodium benzoate as model hydrotropic agents. TLC of these selected poorly water-soluble drugs was performed using mobile phases as per the Indian Pharmacopoeia (IP) 2007 involving the use of organic solvents.

In case of the proposed methods, solutions of sodium benzoate or urea in distilled water were employed as mobile phases to perform TLC of the selected drugs. The observed Rf values in the case of proposed methods ranged from 0.63 to 0.90; while in the case of IP 2007 methods, Rf values ranged from 0.60 to 0.87. The proposed TLC methods were new, simple, cost-effective, environment friendly and safe. In future, hydrotropic solutions shall prove a boon in TLC and high performance thin layer chromatography (HPTLC) analysis of a vast number of drugs discouraging the use of organic solvents to a great extent.

Introduction:

Increasing the aqueous solubility of insoluble and slightly soluble drugs is of major importance. Hydrotropy refers to the ability of a concentrated solution of a chemical compound to increase the aqueous solubility of another compound (usually a poorly water-soluble compound). Compounds that have this property are called ‘hydrotropes’. A large number of hydrotropic agents have been reported to enhance the aqueous solubilities of vast variety of poorly water-soluble drugs.1-17 Maheshwari18-21 is of the opinion that all substances, whether liquid, gas or solid, possesses solubilizing power. Also, the author is of the opinion that hydrotropy is another type of co-solvency.18-21 A large number of poorly water-soluble drugs have been estimated quantitatively by titrimetry and ultra-violet (UV) spectrophotometry using a large number of hydrotropic solutions,1-15 thus, precluding the use of organic solvents.

Experimental:

Materials

The bulk drug samples of atenolol, ibuprofen and caffeine were generously supplied by Alkem

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Laboratories Limited, Mumbai. The gift samples of paracetamol and diclofenac sodium were supplied by Shree Pharmaceuticals, Indore, Madhya Pradesh. All chemicals and solvents used were of analytical grade.

Methods

TLC studies: In case of TLC studies of diclofenac sodium, a mixture containing 100 volumes of toluene, 10 volumes of hexane and 10 volumes of anhydrous formic acid (as per IP 2007) was employed as mobile phase. The detection of spot was done using solution of potassium dichromate in sulfuric acid. In case of proposed methods for TLC studies of diclofenac sodium, hydrotropic solutions of 5M urea and 2M sodium benzoate were employed, separately, as mobile phases. The detection of spot was done using solution of potassium dichromate in sulfuric acid. The Rf values obtained by all the three methods are presented in Table 1.

In case of TLC studies of paracetamol, a mixture containing 65 volumes of chloroform, 25 volumes of acetone and 10 volumes of toluene (as per IP 2007) was employed as mobile phase. The detection of spot was done using iodine chamber. In case of proposed methods for TLC studies of paracetamol, hydrotropic solutions of 5M urea and 0.5M sodium benzoate (spot could not be observed using 2M sodium benzoate solution or 1M sodium benzoate solution as mobile phase) were employed, separately, as mobile phases. The detection of spot was done using iodine chamber. The Rf values obtained by all the three methods are presented in Table 1.

In case of TLC studies of caffeine, a mixture containing 40 volumes of isobutanol, 30 volumes of chloroform, 10 volumes of strong ammonia solution and 3 volumes of acetone (as per IP 2007) was employed as mobile phase. The detection of spot was done using iodine chamber. In case of proposed methods for TLC studies of caffeine, hydrotropic solutions of 5M urea and 2M sodium benzoate were employed, separately, as mobile phases. The detection of spot was done using iodine chamber. The Rf values obtained by all the three methods are presented in Table 1.

In case of TLC studies of ibuprofen, a mixture containing 75 volumes of n-hexane, 25 volumes of ethyl acetate and 5 volumes of glacial acetic acid (as per IP 2007) was employed as mobile phase. The detection of spot was done using iodine chamber. In case of proposed methods for TLC studies of ibuprofen, hydrotropic solutions of 5M urea and 2M sodium benzoate were employed, separately, as mobile phases. The detection of spot was done using iodine chamber. The Rf values obtained by all the three methods are presented in Table 1.

In case of TLC studies of atenolol, a mixture containing 99 volumes of methanol and 1 volume of strong ammonia solution (as per IP 2007) was employed as mobile phase. The detection of spot was done using iodine chamber. In case of proposed methods for TLC studies of atenolol, hydrotropic solutions of 5M urea and 1M sodium benzoate (spot could not be observed using 2M sodium benzoate solution as mobile phase) were employed, separately, as mobile phases. The detection of spot was done using iodine chamber. The Rf values obtained by all the three methods are presented in Table 1.

Table 1: Results of Thin Layer Chromatography

<table>
<thead>
<tr>
<th>S. No.</th>
<th>Drug</th>
<th>Method</th>
<th>Mobile Phase</th>
<th>Rf Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Atenolol</td>
<td>IPM</td>
<td>A mixture of 99 volumes of methanol and 1 volume of strong ammonia solution</td>
<td>0.67</td>
</tr>
<tr>
<td>2.</td>
<td>Atenolol</td>
<td>PM&lt;sub&gt;UR&lt;/sub&gt;</td>
<td>5M urea solution</td>
<td>0.77</td>
</tr>
<tr>
<td>3.</td>
<td>Atenolol</td>
<td>PM&lt;sub&gt;SB&lt;/sub&gt;</td>
<td>1M sodium benzoate solution</td>
<td>0.63</td>
</tr>
<tr>
<td>4.</td>
<td>Diclofenac sodium</td>
<td>IPM</td>
<td>A mixture of 100 volumes of toluene, 10 volumes of hexane and 10 volumes of anhydrous formic acid</td>
<td>0.87</td>
</tr>
<tr>
<td>5.</td>
<td>Diclofenac sodium</td>
<td>PM&lt;sub&gt;UR&lt;/sub&gt;</td>
<td>5M urea solution</td>
<td>0.87</td>
</tr>
<tr>
<td>6.</td>
<td>Diclofenac sodium</td>
<td>PM&lt;sub&gt;SB&lt;/sub&gt;</td>
<td>2M sodium benzoate solution</td>
<td>0.64</td>
</tr>
<tr>
<td>7.</td>
<td>Paracetamol</td>
<td>IPM</td>
<td>A mixture of 65 volumes of chloroform, 25 volumes of acetone and 10 volumes of toluene</td>
<td>0.65</td>
</tr>
<tr>
<td>8.</td>
<td>Paracetamol</td>
<td>PM&lt;sub&gt;UR&lt;/sub&gt;</td>
<td>5M urea solution</td>
<td>0.86</td>
</tr>
<tr>
<td>9.</td>
<td>Paracetamol</td>
<td>PM&lt;sub&gt;SB&lt;/sub&gt;</td>
<td>0.5M sodium benzoate solution</td>
<td>0.68</td>
</tr>
<tr>
<td>10.</td>
<td>Caffeine</td>
<td>IPM</td>
<td>A mixture of 40 volumes of isobutanol, 30 volumes of chloroform, 10 volumes of strong ammonia solution and 3 volumes of acetone</td>
<td>0.70</td>
</tr>
<tr>
<td>11.</td>
<td>Caffeine</td>
<td>PM&lt;sub&gt;UR&lt;/sub&gt;</td>
<td>5M urea solution</td>
<td>0.89</td>
</tr>
<tr>
<td>12.</td>
<td>Caffeine</td>
<td>PM&lt;sub&gt;SB&lt;/sub&gt;</td>
<td>2M sodium benzoate solution</td>
<td>0.87</td>
</tr>
<tr>
<td>13.</td>
<td>Ibuprofen</td>
<td>IPM</td>
<td>A mixture of 75 volumes of n-hexane, 25 volumes of ethyl acetate and 5 volumes of glacial acetic acid</td>
<td>0.60</td>
</tr>
<tr>
<td>14.</td>
<td>Ibuprofen</td>
<td>PM&lt;sub&gt;UR&lt;/sub&gt;</td>
<td>5M urea solution</td>
<td>0.90</td>
</tr>
<tr>
<td>15.</td>
<td>Ibuprofen</td>
<td>PM&lt;sub&gt;SB&lt;/sub&gt;</td>
<td>2M sodium benzoate solution</td>
<td>0.82</td>
</tr>
</tbody>
</table>


Hydrotropy in TLC
mobile phases. The detection of spot was done using iodine chamber. The Rf values obtained by all the three methods are presented in Table 1.

**Results and Discussion:**

As evident from Table 1, the obtained Rf values for *atenolol*, using IP 2007 mobile phase (mostly containing an organic solvent, methanol), 5M urea solution and 1M sodium benzoate solution were 0.67, 0.77 and 0.63, respectively. The obtained Rf values for *diclofenac sodium*, using IP 2007 mobile phase (predominantly containing organic solvents, toluene and hexane), 5M urea solution and 2M sodium benzoate solution were 0.87, 0.87 and 0.64, respectively. The obtained Rf values for *paracetamol*, using IP 2007 mobile phase (mostly containing organic solvents, chloroform, acetone and toluene), 5M urea solution and 0.5M sodium benzoate solution were 0.65, 0.86 and 0.68, respectively.

The obtained Rf values for *caffeine*, using IP 2007 mobile phase (predominantly containing organic solvents, isobutanol, chloroform and acetone), 5M urea solution and 2M sodium benzoate solution were 0.70, 0.89 and 0.87, respectively. The obtained Rf values for *ibuprofen*, using IP 2007 mobile phase (predominantly containing organic solvents, n-hexane and ethyl acetate), 5M urea solution and 2M sodium benzoate solution were 0.60, 0.90 and 0.82, respectively.

It is, thus, well observed that the Rf values obtained employing the proposed methods using the hydrotropic solutions as mobile phases was satisfactory. The proposed methods were devoid of tailing effect. The hydrotropic resolution also showed advantage of absence of tailing and time effectiveness as that of the standard solvent system.

**Conclusion:**

It may, thus, be concluded that the proposed method of analysis was new, simple, cost-effective, environment-friendly and safe. The decided advantage was that the organic solvents were precluded, but not at the expense of accuracy. The proposed method can be successfully employed in the TLC of other drugs, as well. It is expected that the hydrotropic solution systems can be employed in HPTLC analysis in future and can be developed as a novel tool to eliminate the use of expensive, pollutant and toxic organic solvents.

**Acknowledgments:**

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**Abbreviations:**

- **HPTLC** = High Performance Thin Layer Chromatography.
- **IP** = Indian Pharmacopoeia.
- **IPM** = Indian Pharmacopoeial Method (2007).
- **PMSB** = Proposed Method Using Sodium Benzoate Solution.
- **PMUR** = Proposed Method Using Urea Solution.
- **TLC** = Thin Layer Chromatography.
- **UV** = Ultra-Violet.

**References:**