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Research Article

HYDROTROPY: A NOVEL APPROACH IN ESTIMATION OF POORLY AQUEOUS SOLUBLE DRUGS BY TLC

JAYRONIA SONALI[b], YADAV KAMALDEEP[b], SHARMA BHUMIKA[b], JAIN SANJAY[b], MAHESHWARI RAJESH KUMAR[a]

[a]Shri G S Institute of Technology and Science, 23 Park Road, Indore- 452003 (MP) India, [b]Smriti College of Pharmaceutical Education, 4/1 Piplia Kumar Kakad, Maya Khedi Road, Indore 452010, (MP), India. Email: jayroniasonali5@gmail.com

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ABSTRACT

The thin layer chromatography (TLC) of drugs are usually performed with the help of solvents like butyl amine, toluene, ether, chloroform, light petroleum, ethyl acetate, ethanol, hexane, xylene and phenol, most of which are much expensive and toxic. In the present study, hydrotropic agents are employed as mobile phase for estimation of poorly aqueous soluble drugs by TLC technique. Erythromycin, Ciprofloxacin and Norfloxacin were selected as model drugs for estimation by TLC and Sodium Benzoate, urea, and Sodium Salicylate were taken as hydrotropic agents for mobile phase. TLC of selected model drugs were also performed by using proposed method given in Indian Pharmacopoeia (IP).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 thereby limiting the use of organic solvents to a great extent.

Keywords: Thin layer Chromatography, Erythromycin, Ciprofloxacin, Norfloxacin, Hydrotropic solutions.

INTRODUCTION

The term hydrotropic agent was first introduced by Neuberg (1916), to designate anionic organic salts. According to Neuberg, hydrotropic agents are metal salts of organic acids which at fairly high concentration considerably increase the aqueous solubility of organic substances normally slightly soluble in water. [1][2]

According to Saleh and El-Khordagui, hydrotropic agents are freely soluble organic compounds which at a concentration sufficient to induce a stack-type aggregation considerably enhance the aqueous solubility of organic substances, practically insoluble under normal conditions. These compounds may be anionic, cationic or neutral molecules. However, the term has been used in the literature to designate non micelle forming substances either liquids or solids, organic or inorganic capable of solubilizing insoluble compounds. [3]

Hydrotropy refers to the ability of a concentrated solution of a chemical compound to increase the aqueous solubility of another compound (usually a sparingly soluble organic compound). Compounds that have this property are called 'hydrotropes'. [4-12] Hydrotropic agents are structurally characterized by having a short, bulky, compact moiety such as an aromatic ring, while surfactants are characterized by long hydrocarbon chains. In general hydrotropic agents have a shorter hydrophobic segment, leading to higher water solubility, than do surfactants [13-14]

Examples of hydrotropic agents used as excipients in the literature are urea, sodium salicylate, sodium gentisate, sodium gluconate, sodium benzoate, sodium ascorbate, sodium citrate, sodium ibuprofen, pheniramine, lysine, tryptophan, sodium acetate and isoniazid. Each hydrotropic agent is effective in increasing the water solubility of selected hydrophobic drugs; no universal hydrotropic agent has been found effective to solubilize all hydrophobic drugs. Thus, finding the right hydrotropic agents for a poorly soluble drug requires screening a large number of candidate hydrotropes. [13-15]

Advantages of Hydrotropic Solubilization [13]

- Hydrotropy is suggested to be superior to other solubilization methods, such as micellar solubilization, miscibility, cosolvency and salting in, because the solvent character is independent of pH, has high selectivity and does not require emulsification. It only requires mixing the drug with the hydrotrope in water.
- It does not require chemical modification of hydrophobic drugs, use of organic solvents, or preparation of emulsion system.
- Economic, safe, environmental friendly and user friendly method.

The present investigation demonstrates the application of hydrotropy for chromatographic estimation of selected model drugs. Hydrotropic agents are employed as mobile phase for estimation of poorly aqueous soluble drugs by TLC technique. Erythromycin, Ciprofloxacin and Norfloxacin are selected as model drugs for estimation by TLC and Urea, Sodium Benzoate and Sodium Salicylate were selected as hydrotropic agent for mobile phase. TLC of selected model drugs were also performed by using proposed method as per the method given in Indian Pharmacopoeia (IP).

MATERIALS AND METHOD

Materials

The bulk drug samples of Erythromycin, Ciprofloxacin and Norfloxacin were procured from Unichem Laboratories Limited, Mumbai. All chemicals and solvents used were of analytical grade.

Method

Thin layer chromatography of the drugs were carried out on TLC glass plates, precoated with silica gel G (Renkem) using different organic solvent systems and hydrotropic solutions. And the plates were visualized in the UV short and long radiation and also treated with Iodine vapours. The Rf values of spots were calculated by using the following formula:

Rf = Distance Moved by solute/distance moved by the mobile phase front

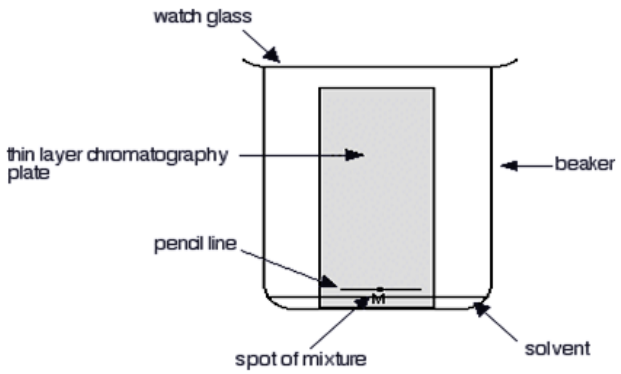
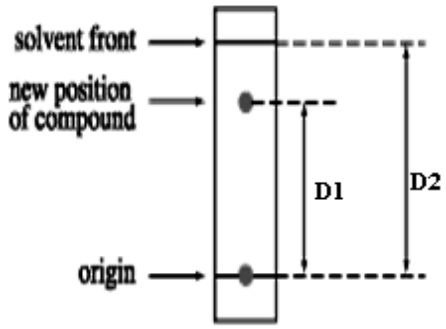


Fig. 1: Developing chamber for thin layer chromatogram



Rf = D1/D2 =

Fig. 2: TLC plate showing distances traveled by the solute and the solvent after solvent front nearly reached the top of the adsorbent

TLC studies

- In T.L.C study of ***Erythromycin*** a mixture of solvent containing 45 volumes of ethylacetate, 40 volumes of 15% w/v of ammonia acetate and 20 volume of 2-propanol as per IP were used as a mobile phase. The detection of spot was carried out under UV light. In proposed method for T.L.C studies of ***Erythromycin,*** hydrotropic solution of 2M urea and 2M sodium benzoate were used as a mobile phase and the detection of spot was carried out under UV light the Rf value obtained by all the method are presented in table1.

- In T.L.C study of ***Ciprofloxacin*** mixture of solvent containing 40 volume of dichloromethane, 40 volume of methanol, 20 volume of strong ammonia and 10 volume of acetonitrile as per IP were used as a mobile phase .The detection of spot was carried out under UV light. In proposed method for T.L.C studies of ***Ciprofloxacin,*** hydrotropic solution of 2M sodium benzoate and 2M sodium salicylate were used as a mobile phase and the spot was detected under UV light. The Rf value obtained by all the method are presented in table1.

- In T.L.C study of ***Norfloxacin*** mixture of solvent containing 40 volume of dichloromethane, 40 volume of methanol 20 volume of toluene, 14 volume of diethylamine and 8 volume of water as per IP were used as a mobile phase .The detection of spot was carried out under UV light. In proposed method for T.L.C studies of ***Norfloxacin,*** hydrotropic solution of 2M urea and 2M sodium benzoate were used as a mobile phase and the spot was detected under UV light. The Rf value obtained by all the method are presented in table 1.

Table 1: Results of Thin Layer Chromatography

S. No.	Drugs	Method	Mobile phase	Rf value
1	Erythromycin	IPM	Mixture of solvent containing 45 volumes of ethylacetate,40 volumes of 15% w/v of ammonia acetate and 20 volume of 2-propanol	0.87
2	Erythromycin	PM^{U}	2M urea	0.92
3	Erythromycin	PM^{SB}	2M sodium benzoate	0.93
4	Ciprofloxacin	IPM	Mixture of solvent containing 40 volume of dichloromethane,40 volume of methanol, 20volume of strong ammonia and 10 volume of acetonitrile	0.63
5	Ciprofloxacin	PM^{SB}	2M sodium benzoate	0.53
6	Ciprofloxacin	PM^{SS}	2M sodium salicylate	0.69
7	Norfloxacin	IPM	Mixture of solvent containing 40 volume of dichloromethane,40 volume of methanol, 20 volume of toluene, 14volume of diethylamine and 8 volume of water	0.88
8	Norfloxacin	PM^{U}	2M urea	0.81
9	Norfloxacin	PM^{SB}	2M sodium benzoate	0.90

IPM = Indian pharmacopoeial method 2007, PM^{U} = proposed method using solution of urea, PM^{SB} = proposed method using solution of sodium benzoate, PM^{SS} =proposed method using solution of sodium salicylate

RESULTS AND DISCUSSION

As explained in table 1, the Rf value obtained for ***Erythromycin*** using IP 2007 mobile phase containing an organic solvents, 2M urea and 2M sodium benzoate were 0.87, 0.92, 0.93 respectively. **T**he Rf value obtained for ***Ciprofloxacin*** using IP 2007 mobile phase containing an organic solvents, 2M sodium benzoate, 2M sodium salicylate were 0.63, 0.53, 0.74 respectively . The Rf value obtained for ***Norfloxacin*** using IP 2007 mobile phase containing an organic solvents, 2M urea, and 2M sodium benzoate were 0.88, 0.81, 0.90 respectively. Thus the Rf values obtained by proposed methods using the hydrotropic solutions as mobile phase are satisfactory. Thus the tailing effect in proposed method was not observed.

CONCLUSION

It may, thus, be concluded that the proposed method of analysis is new, simple, cost-effective, Environment-friendly and safe. 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 other analytical technique like HPTLC etc. in future and can be developed as a novel tool to eliminate the use of expensive, pollutant and toxic organic solvents.

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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.

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