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ECOFRIENDLY APPLICATION OF MIXED HYDROTROPY TO CARRYOUT THIN LAYER CHROMATOGRAPHY OF COMPOUNDS WITHOUT THE INVOLVEMENT OF ORGANIC SOLVENTS

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Abstract: Many organic solvents namely butanol, acetic acid, ethyl acetate, chloroform, cyclohexane, methanol, ether, acetonitrile, toluene, dichloromethane, benzene and carbon tetra chloride are used to perform thin layer chromatography (TLC) of various drugs. Most of these organic solvents are harmful to health and are expensive. Some of these organic solvents are carcinogenic. Organic solvents are responsible for polluting the environment also their disposal from laboratories, industries etc. require special procedure which makes the process more tedious and costly. In the present research work mixed hydrotropic solutions were used as mobile phases to perform TLC of the drugs, precluding the use of organic solvents. Ciprofloxacin hydrochloride, Thiamine hydrochloride, Metformin hydrochloride, Lignocaine hydrochloride were selected as model drugs. Sodium benzoate, sodium citrate, sodium acetate and urea in various combinations were used as model hydrotropic agents. The solutions of above mentioned hydrotropic agents in distilled water in different concentrations were used as mobile phases to perform TLC of selected drugs. The R_f values so obtained in the proposed methods ranged from 0.19 to 0.84. As per mixed solvency concept, all molecules present in this universe possess solubilizing properties. In this particular research, a green method has been explored utilizing the solubilizing properties of solids. We can replace harmful organic solvents in this way.

KEYWORDS: Hydrotropic agents, Hydrotropic solubilization, Mixed hydrotropy, Thin Layer Chromatography, Organic solvents.

INTRODUCTION:

Hydrotropic solubilization has major importance in increasing the aqueous solubility of insoluble and slightly soluble drugs. Hydrotropy is defined as the ability of a concentrated solution of a chemical compound to increase the aqueous solubility of a poorly water-soluble compound. Compounds having this property are termed as hydrotrops. Hydrotropy is considered superior than other solubilization techniques like co-solvency and micellar solubilization because the solvent character does not depend on pH, has more selectivity and emulsification is certainly not required. Requirement is just to mix the drug with the hydrotrope in water. The phenomenon in which there is an increase in the solubility of poorly water-soluble drugs employing blends of hydrotropic agents is called Mixed hydrotropic solubilization. This technique helps in providing synergistic and additive effect on increasing the solubility of poorly water-soluble drugs. Many hydrotropic agents are known which increase the aqueous solubilities of a wide range of poorly water-soluble drugs, as a result use of organic solvents is not required. Hydrotropic and mixed hydrotropic solubilization techniques can be taken in account for pharmaceutical formulations and in a variety of techniques of analysis such as UV spectrophotometric analysis, titrimetric analysis, high-performance liquid chromatography (HPLC) and thin layer chromatography (TLC).

The technique used to separate mixture of chemical substances into its individual compounds is called thin layer chromatography. Chromatography involves two phases: one mobile phase and one stationary phase. TLC plate which is the stationary phase is prepared with the mixture of silica gel and water. A suitable solvent (mobile phase) is used to move along with compound mixture through the TLC plate according to the degree of adhesion and polarity of each component on the stationary phase.

Solutions which contain hydrotropic agents (hydrotropic and mixed hydrotropic solutions) can be used as mobile phases in different ratios so as to adjust polarity or non-polarity and to achieve the results with tailing effects as low as possible. Hydrotropic solubilization, Mixed hydrotropic solubilization and Mixed solvency concept have been used for the enhancement of aqueous solubility of large number of poorly water-soluble drugs. (1-35). As per mixed solvency concept, all molecules present in this universe possess solubilizing properties. In this particular research, a green method has been explored utilizing solubilizing properties of solids. We can replace harmful organic solvents in this way.

MATERIALS:

Silica gel GF 254 for thin layer chromatography was obtained from Merck Specialities Pvt Ltd, Worli, Mumbai.

Metformin HCl, was obtained from IPCA Laboratories, Ratlam. Ciprofloxacin HCl, Lignocaine HCl, and Thiamine HCl were obtained from Modern Laboratories, Indore.

Sodium acetate, Sodium benzoate, Sodium citrate and Urea used were of analytical grade.

METHOD:

A suspension of silica gel GF 254 was prepared in distilled water and was uniformly spread on the glass slides 7cm long. The thickness was maintained between 0.25 to 0.30mm. The coated plates were dried in hot air oven at 100-1500C for about an hour.

Six different types of mobile phases were prepared by dissolving various hydrotropic agents in distilled water. For example; Blend 1 was prepared by initially dissolving 2gm of sodium acetate, 2gm of sodium benzoate, 2gm of sodium citrate, and 2gm of urea in 40ml of distilled water using vortex apparatus. Then, the volume was made up to 100ml with distilled water. The remaining blends were prepared similarly by dissolving different proportions of the hydrotropic agents (Table1). Drug solutions of 2% w/v concentration were prepared using distilled water as solvent. Drug (200mg) was taken with 4-6 ml of distilled water in 10ml of volumetric flask for dissolving the drug which was then shaken using vortex apparatus for complete dissolution and then the volume was made up to 10ml with distilled water. These solutions were used to put the spots on TLC plates using capillary tubes. The solvent (water) was removed by heating the plates in hot air oven at 100-1500C.

TLC Studies - Thin layer chromatography of the sample drugs was carried out on prepared silica gel GF 254 TLC glass plates using different mixed hydrotropic solutions as mobile phases. Plates were developed in such a way that solvent front travelled about 75-80% portion of the plates. The developed TLC plates were kept in oven at 100-1500C for nearly 60 minutes for removal of water**.**

Table 1: Composition of different mixed hydrotropic solutions (mobile phases)

Blend 1	2% SA+ 2% SB+ 2% SC+ 2% U
Blend 2	4% SA+ 2% SB+ 4% U
Blend 3	2% SB+ 4% SC+ 4% U
Blend 4	2% SA+ 4% SB+ 4% SC
Blend 5	3% SA+ 5% SB+ 2% SC
Blend 6	2% SA+ 5% SB+ 3%SC

(SB- Sodium Benzoate, SA- Sodium Acetate, SC- Sodium Citrate, U- Urea)

The spots of the drugs were observed under UV chamber. The Retention factor (R_f) values of drug spots were calculated using the given formula:

R_f = Distance travelled by solute front/ Distance travelled by the solvent front.

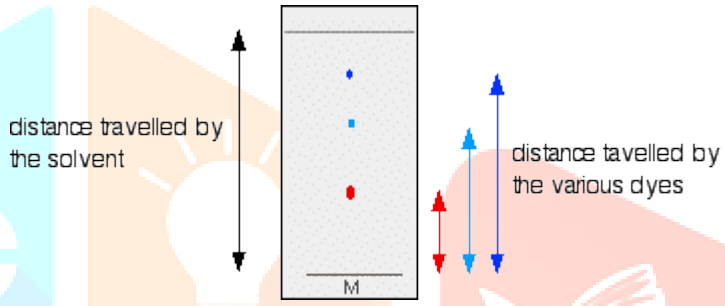
The R_f values of different drugs so obtained are mentioned in Table 2.

Table 2: Results of TLC studies

S.no.	Drug	Blend	R_f Value
1	Ciprofloxacin hydrochloride	Blend 5 (5% SB, 2% SC, 3% SA)	0.61
		Blend 6 (5% SB, 3% SC, 2% SA)	0.66
2	Lignocaine hydrochloride	Blend 4 (4% SB, 4% SC, 2% SA)	0.40
3	Metformin hydrochloride	Blend 3 (2% SB, 4% SC, 4% U)	0.19
		Blend 5 (5% SB, 2% SC, 3% SA)	0.62
4	Thiamine hydrochloride	Blend 4 (4% SB, 4% SC, 2% SA)	0.39
		Blend 6 (5% SB, 3% SC, 2% SA)	0.71

(SB- Sodium Benzoate, SC- Sodium Citrate, SA- Sodium Acetate, U- Urea)

Note: Results in which tailing effects were observed are not mentioned in Table 2.



$$R_f = \frac{Distance\ travelled\ by\ component}{Distance\ travelled\ by\ solvent}$$

RESULT AND DISCUSSION

It is well observed that the Rf values obtained after employing the proposed methods using the mixed hydrotropic solutions as mobile phases were satisfactory. The selected mobile phases (mentioned in Table2) gave good results with almost negligible tailing effect.

As evident from Table2, Blend 5 and Blend 6 were found suitable mobile phase for TLC of Ciprofloxacin HCl, spots did not show tailing effect. The Rf value obtained were 0.61 and 0.66 using Blend 5 and Blend 6, respectively.

Blend 4 was found suitable mobile phase for TLC of Lignocaine HCl, spots did not show tailing effect. The Rf value obtained was 0.40 using Blend 4.

Blend 3 and Blend 5 were found suitable mobile phase for TLC of Metformin HCl, spots did not show tailing effect. The Rf value obtained were 0.19 and 0.62 using Blend 3 and Blend 5, respectively.

Blend 4 and Blend 6 were found suitable mobile phase for TLC of Thiamine HCl, spots did not show tailing effect. The Rf value obtained were 0.39 and 0.71 using Blend 4 and Blend 6, respectively.

TLC and HPTLC studies are largely conducted in various colleges (institutions), laboratories, forensic science laboratories, chemistry laboratories, pharmacy laboratories, chemical industries, pharmaceutical industries, government analytical laboratories etc. All TLC/HPTLC studies involve the use of organic solvents like methanol, heptane, tetrahydrofuran, toluene, di-ethylamine, chloroform, ethyl acetate, ethanol, dichloromethane, and hexane. Most of the organic solvents mentioned are expensive and their exposure to human being is harmful and also the elimination of such solvents is arduous. Some of them also act as carcinogens. In the present investigation the use of these organic solvents has perfectly been replaced with harmless and economically feasible hydrotropic agents.

CONCLUSION

Hence it can be inferred from the results above that the methods proposed are simple, economically feasible, eco-friendly, and safe. The biggest advantage is that it precludes the usage of organic solvents. Also the proposed methods can also be successfully used in the TLC of other drugs, as well. The proposed methods can also be employed in the HPTLC analysis in future to eliminate the use of expensive and toxic organic solvents which are also harmful for the environment.

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