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Hydrotropic Mobile Phases: A Sustainable and Efficient TLC Approach for Acetaminophen Analysis

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Abstract- **The present research study introduces a novel mixed hydrotropic solvent system as an alternative green chemistry based mobile phase for the Thin Layer Chromatography (TLC) separation of acetaminophen. Traditional TLC solvents are often associated with high toxicity, volatility, and environmental burden. The study utilized sodium benzoate, thiourea and sodium salicylate in aqueous systems as effective hydrotropes for the development of a mobile phase. The hydrotropic mixture in 1:2:1 (sodium salicylate: thiourea: sodium benzoate) was compared with the conventional mobile phase and results showed comparable results, with proposed hydrotropic blend offering better environmental and cost profiles. These findings suggest a viable, sustainable, and non-toxic alternative to traditional organic solvents used in pharmaceutical analysis.**

Keywords: Thin Layer Chromatography, Hydrotropes, Green Chemistry, Eco-friendly Solvents

I. INTRODUCTION

Thin Layer Chromatography (TLC) is a widely used analytical technique used for qualitative as well as quantative assessment of chemical compounds in pharmaceutical quality control due to its simplicity, speed, and cost-effectiveness [1]. Unlike other analytical methods, TLC needs minimal equipment and provides flexible way for impurity profiling and routine analysis [2].

However, the conventional TLC uses organic solvents such as chloroform, acetone, and methanol which pose documented health and environmental risks including risks of inhalation toxicity, carcinogenicity, flammability, and ecological contamination due to their toxic and volatile nature [3]. The increasing demand for green chemistry has also driven the developments of greener alternatives to decrease ecological footprints while maintaining good analytical performance [4]. It is in this context that the hydrotropes (a class of water-soluble organic compounds well known for increasing the solubility of poorly soluble substances) have become an appealing strategy in the field of sustainable analytical chemistry. Hydrotropes are biodegradable and less toxic as compared to the conventional solvents [5]. Mixed hydrotropy is extension of hydrotropic solubilization where instead of using single hydrotrope, mixture of hydrotropic agents is used in definite ratios to get synergistic effects [6]. Mixed hydrotrophy has been employed in TLC with positive results [7], the current study explores the formulation of hydrotropic mobile phases using sodium benzoate, sodium salicylate, and thiourea, aiming to replace traditional organic solvent systems in the TLC separation of acetaminophen.

II. MATERIAL AND METHODOLOGY

2.1 Materials

- Drug Standard: Acetaminophen (Paracetamol)
- Hydrotropes: Sodium salicylate, thiourea, and sodium benzoate (1:2:1 ratio)
- TLC Plates: Pre-coated silica gel GF254
- Instrumentation: Glass development chamber; iodine vapor chamber for spot visualization

2.2 Preparation of Hydrotropic Mobile Phases

A mixed hydrotropic mobile phase was formulated by dissolving sodium salicylate, thiourea, and sodium benzoate in a 1:2:1 weight ratio in distilled water to achieve a final concentration of 30% w/v. The mixture was stirred until a clear solution was obtained. Binary systems were initially screened, but the ternary 1:2:1 combination yielded the most effective separation and stability.

Conventional TLC mobile phase was prepared using Chloroform: Acetone (9:1 v/v) [8].

2.3 TLC Procedure

Standard solutions of acetaminophen were prepared in distilled water and applied to TLC plates using a calibrated micropipette.

The plates were developed in a saturated chamber containing the hydrotropic mobile phase. After development, the plates were dried and exposed to iodine vapor for spot visualization. The brown spots corresponding to acetaminophen were marked, and their retention factor (Rf) values were calculated.

Same procedure was followed for conventional mobile phase and retention factor (Rf) was calculated and compared with hydrotropic based solvent phase.

2.4 Evaluation Parameters

- Separation Efficiency: Assessed based on clarity, compactness, and resolution of acetaminophen spots.
- Stability: Mobile phase was stored in sealed containers at room temperature and evaluated at 0, 5, 10, and 15-day intervals.
- Eco-friendliness: Evaluated qualitatively based on the absence of volatile organic compounds, toxicity data from literature, and compliance with green chemistry principles.
- Cost-effectiveness: Estimated through comparative pricing of hydrotropes versus acetone and chloroform, and analysis of reagent consumption per TLC run.

III. RESULTS AND DISCUSSION

3.1 Retention Factor (Rf) and Separation Efficiency

The TLC analysis of acetaminophen using the novel hydrotropic mobile phase (sodium salicylate: thiourea: sodium benzoate, 1:2:1) demonstrated sharp, distinct, and compact brown spots upon exposure to iodine vapor. The Rf values were consistent across replicates and exhibited good reproducibility.

In comparison, the conventional mobile phase (chloroform: acetone, 9:1 v/v) also produced acceptable separation; however, the spot diffusion was slightly broader, and solvent handling required precautions due to volatility and toxicity.

3.2 Comparison of TLC Parameters

Parameter	*Conventional Mobile Phase*	*Hydrotropic Mobile Phase*
Rf Value (Mean ± SD)	0.52 ± 0.02	0.50 ± 0.01
Spot Clarity	Moderate	Sharp and compact
Solvent Toxicity	High (inhalation risk, carcinogenic potential)	Low (biodegradable, GRAS status)
Volatility/Flammability	High	Negligible
Stability Over 15 Days	Moderate (chloroform loss observed)	Stable, no degradation
Cost per 100 mL	Approx. ₹80–₹100	Approx. ₹25–₹30
Environmental Impact	Hazardous waste generation	Minimal ecological burden
Detection Method	iodine vapor	Iodine vapor

The Rf value of acetaminophen with the hydrotropic mobile phase was measured at 0.50 ± 0.01, which is comparable to the conventional system (0.52 ± 0.02). Importantly, the spot resolution in the hydrotropic system was slightly sharper, indicating better phase–solute interaction, potentially due to hydrogen bonding and synergestic effects of the hydrotropic matrix.

3.3 Reproducibility and Storage Stability

The hydrotropic mobile phase remained stable over a 15-day observation period. No visible precipitation, pH shift, or microbial growth was noted. Rf values measured on Days 0, 5, 10, and 15 showed insignificant variation ($\Delta Rf < 0.02$), confirming stability for extended routine use in laboratories. In contrast, chloroform-based systems showed partial evaporation and solvent loss, requiring tightly sealed containers and cold storage to prevent degradation.

3.4 Environmental and Economic Considerations

Conventional TLC solvents like chloroform and acetone are classified under hazardous chemicals due to their carcinogenic, flammable, and volatile nature, requiring strict handling and disposal protocols. Conversely, sodium salicylate, thiourea, and sodium benzoate are non-volatile, water-soluble, biodegradable, and recognized as Generally Recognized as Safe (GRAS) by regulatory agencies, making them significantly safer for laboratory personnel and the environment.

Cost analysis revealed that hydrotropic mobile phases are up to 65% more economical per 100 mL compared to solvent-based systems, especially when factoring in storage and disposal requirements. This positions hydrotropic systems as both environmentally and economically sustainable.

3.5 Advantages of Hydrotropic System

- Comparable Rf values to conventional TLC systems
- Excellent spot clarity and resolution
- Improved safety profile and reduced regulatory burden
- Lower cost and high stability during storage
- No flammable or carcinogenic constituents
- Aligns with the principles of green analytical chemistry.

IV. CONCLUSION-

The research study strongly suggest that the novel mixed hydrotropic mobile phase composed of sodium salicylate, thiourea, and sodium benzoate (1:2:1) can be green alternative to conventional organic solvent systems in the TLC separation of acetaminophen. The hydrotropic based solvent system further reduced both the toxicity, and volatility and environmental hazard of the organic system. These findings not only validate the analytical potential of hydrotropic systems but also emphasize their applicability in routine pharmaceutical quality control, where safety, sustainability, and cost-effectiveness are critical. Future studies may extend this approach to a broader range of pharmaceutical compounds, paving the way for the widespread adoption of eco-friendly solvent systems in chromatographic techniques.

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