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Applicability of Deep Eutectic Solvent as a Sustainable Reaction Medium in Biocatalytic Multicomponent Synthesis

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Abstract

Over the last decade, deep eutectic solvents (DESs) have gained recognition as a promising alternative to conventional organic solvents, from both environmental as well as technological perspectives. Due to its inherent biological properties these eutectic solvents serve as ideal reaction media with whole cells and isolated enzymes which have shown improved enzyme stability and activity translating to high conversion of product. In this article, we have reported Baker's yeast (*saccharomyces cerevisiae*) catalyzed one-pot three component condensation of aryl aldehydes, thioglycolic acid, and amines in deep eutectic solvent leading to 4-thiazolidinones successfully. This article presents a successful one-pot three-component condensation of aryl aldehydes, amines and thioglycolic acid, catalyzed by Baker's yeast (*Saccharomyces cerevisiae*) in a deep eutectic solvent, leading to the efficient synthesis of 4-thiazolidinones. The chloride-based deep eutectic solvent (DES) used in this methodology can be effectively reused and recycled up to five consecutive runs without any significant loss in catalytic activity.

Keywords: Deep eutectic solvents, biocatalysis, thiazolidinones, sustainable and greener synthesis

Introduction

Over the past few decades, biocatalysis has gained significant importance in organic transformations due to its eco-friendly nature, enabling reactions under mild and sustainable conditions while minimizing the use of hazardous chemicals ^[1-4]. Enzymes offer high regioselectivity, chemoselectivity and stereoselectivity, making them ideal for producing pure compounds, particularly in pharmaceuticals ^[5]. Derived from renewable sources, biocatalysts are cost-effective, biodegradable and energy efficient ^[2]. Biocatalysts have broad substrate scopes and are well suited for large-scale manufacturing processes, further emphasizing their value in green and efficient chemical transformations. Whole-cell biocatalysis by using yeast has demonstrated significant applicability in the field of pharmaceutical and medicinal chemistry. Notably, the whole-cell or enzymatic transformations have also been reported under non-aqueous conditions, including in ionic liquids or neat substrates among other solvent-free reaction media ^[4, 6] To improve the solubility of substrates and products, the usage of non-conventional reaction media in biocatalysis provides a practical and enzyme-compatible framework. Various ILs have demonstrated efficiency in biocatalytic processes; though, their application is limited by concerns related to high-cost and toxicity ^[4, 7]. To overcome these challenges, deep eutectic solvents (DESs) have recently emerged as a new generation of ionic liquids, offering customizable properties making them a promising alternative ^[8-10].

Baker's yeast or *Saccharomyces cerevisiae* can carry out several organic transformations under mild reaction conditions ^[11]. It is available easily, economical and non-hazardous. Baker's yeast and lipase can catalyze several condensation reactions to synthesize biologically active structurally diverse heterocyclic compounds like polyhydroquinolines ^[12], dihydropyridines ^[13], dihydropyrimidines ^[14], benzotriazoles ^[15],