

## Green, eco-friendly bio-analytical techniques for pharmaceutical analysis.

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### Introduction

Analytical chemistry plays an important role in pharmaceutical research. It is involved in different stages of drug manufacturing such as analysis of active ingredients, separation of enantiomers or impurities in bulk drugs and pharmaceutical formulations [1]. Bio analytical methods play an important role in the quantitative evaluation of drugs and their metabolites in physiological matrices such as blood, plasma, serum, or urine. Greening the analytical methods is gaining high interest among researchers. Because of the monetary and ecological impact of using large amounts of organic solvents and waste disposal, the analytical community are directed to implement the principles of green analytical chemistry (GAC) in analytical laboratories and to substitute polluting analytical methodologies with green ones [2]. However, various techniques can be used for the bio analysis of pharmaceuticals, liquid chromatography is still the most popular technique used in commercial and research laboratories [3]. Chromatographic techniques have the potential to be greener at all steps of the analysis, from sample collection to separation. Different approaches could be used for making liquid chromatographic methods more eco-friendly such as using high speed liquid chromatography, superheated water chromatography, enhanced fluidity liquid chromatography, micellar liquid chromatography, miniaturized instruments, direct liquid chromatography and replacing toxic reagents with green alternatives [4].

Successful trials for greening bio-analytical methods are well documented in the literature. For example, green, eco-friendly UPLC methods were developed for the analysis of various classes of pharmaceuticals in biological fluids using columns packed with fully porous sub-2  $\mu\text{m}$  particles and superficially porous particles. The use of small particle size packing (sub 2  $\mu\text{m}$ ) could enhance the chromatographic performance and reduce the analysis time [5]. The high column backpressure induced by these particles could be overcome by using these particles in combination with UPLC systems.

Several applications of using UPLC–UV, UPLC–MS and UPLC–MS/MS (Quadropole and time-of-flight mass analyzer) methods with columns packed with sub-2  $\mu\text{m}$  particles in bio analysis of pharmaceuticals are reported [6,7]. Another approach for greening bio analysis is the use of superficially porous particles (fused-core particles). These particles could reduce the analysis times while maintaining column efficiencies with relatively low back pressures. The use of fused-core particles for the analysis of pharmaceuticals in biological fluids is well documented in the literature [8-10].

Direct analysis is another approach for greening liquid chromatography and the used direct LC methods for the bio-analysis of pharmaceuticals is also reported [11-13]. For example, Strano-Rossi et al. developed a UHPLC–ESI-MS/MS method for the direct analysis of 14 drugs of abuse in oral fluids with no sample preparation [14]. Miniaturization is also one of the recent methods for greening bio analytical techniques and its applications in bio analysis is well documented [15,16]. In addition, two-dimensional liquid chromatographic separations are applied for the identification and quantification of drugs and their metabolites in biological fluids such as plasma or urine [17].

Greening bio analytical techniques and replacing the existed methods with green ones are expected in the coming years with the aim of minimizing the ecological impacts of the consumption of large amounts of solvents and waste disposal.

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