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Review

Experimental design of supercritical fluid extraction – A review

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ABSTRACT

Supercritical fluid extraction (SFE), a sustainable green technology leads a wide range of applications since the past decade. Like many other processes, SFE is sometimes criticized for its large number of factors which need to be properly adjusted before every single run. Experimental design and proper statistical analysis with small number of trials in adjusting the SFE parameters become popular in this regard. This paper is aimed to review the common experimental designs that are frequently used in the SFE process. Utilizations of different experimental designs in SFE with the intention of either screening the most influential factors or optimizing the selected factors are briefly reviewed. Strategies and recommendation addressing the choice of appropriate design, constructing design matrix, experimental trial and data analysis are discussed in this paper. For more application oriented readers of SFE, an effective and easy chart on choosing proper experimental design and a list of experimental design software are also included.

Contents

1. Introduction

Experimental designs are being frequently used for the optimization of different operating conditions of various processes and for improving the chromatographic separation performance, as well as achieving high extraction efficiency (Hibbert, 2012; Dejaegher and Vander Heyden, 2011; Hanrahan and Lu, 2006; Ferreira et al., 2007a). Theoretically, a number of factors have simultaneous effect on a process. However, application of experimental design is the most effective way to identify and optimize the significant factors, and to achieve a competent result by few experimental trials.

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Table 1
Changeable parameters of SFE in compared with Soxhlet extraction method (adapted from Caude and Thiébaut, 1999).

SFE	Soxhlet extraction
Solvent choice	Solvent choice
Temperature	Particle size of sample
Pressure	Extraction time
Extraction time	
Solvent flow rate	
Sample size	
Extraction time	
Use of modifier	

Therefore, the experimental design can be defined as an approach to solve the problem systematically and, it is applied to collect data and to analyze data for obtaining information-rich result (Gooding, 2004). Optimum and valid results with a minimum effort, time and resources are the primary objectives of applying the experimental design in analytical process (Montgomery, 2004; Cornell, 2011; Myers and Montgomery, 2002). In an experimental design, investigators deliberately maneuver one or several predetermined factors to know their impact on experimental outcome.

Supercritical fluid extraction (SFE) is based on the solvating properties of supercritical fluid (SF), which can be obtained by employing pressure and temperature above the critical point of a compound, mixture or element. Extraction by SF depends on some intrinsic tunable natures of supercritical fluid like temperature, pressure and some extrinsic features like the characteristics of the sample matrix, interaction with targeted analysts and many environmental factors (Cavalcanti and Meireles, 2012; Pereira and Meireles, 2010). A single SFE condition cannot generate enough information addressing all the affecting factors of SFE process. To overcome this difficulty, a large number of variables need to be carefully identified and investigated (Diaz and Brignole, 2009; Espinosa et al., 2000; Diaz et al., 2000). By proper controlling of SFE parameters, the extractability of supercritical fluid can also be modified which enable this process to find its field from food to pesticide researches (Azmir et al., 2013; Khosravi-Darani, 2010; Brunner, 2010; Herrero et al., 2010). Moreover, a higher degree of freedom can be obtained in extraction by SFE than the conventional methods, which means the number of tunable properties goes higher in SFE. Thus, the tunable properties of SFE make this process more unique, sensitive and specific in compared with conventional extraction methods. Table 1 shows a comparison of adjusting parameters of SFE with traditional Soxhlet extraction process.

SFE is regarded as a green process because it does not use chemical solvents with drastic environmental impacts. Some applications of SFE have already been commercialized and some are emerging (Machida et al., 2011). But still now it is considered as a "black box design" of process, because of the complex interaction of affecting factors and lack of knowledge on the in-depth fluid dynamics of supercritical fluid in extraction (Wang et al., 2010). Simple approximations of experimental units are possible to construct in this "black box design", but detail point-to-point process and extraction principle are beyond measurable. Thus, experimental designs are applicable to consider many influential variables and to generate reasonable result of interest without considering the unknown principle of SFE process. A graphical illustration of the position of SFE regarding numerous influential factors and the estimation of outcome by experimental design is shown in Fig. 1. According to Fig. 1, some controlling variables i.e. x_1, x_2, x_3, x_4; some response variables i.e. y_1, y_2, y_3, y_4 and some noisy variables i.e. z_1, z_2, z_3, z_4 co-exist in a black box process. The objective of experimental designs is to optimize the response variables of a certain sample by systematic modification of controlling variables. The design does not consider the variability in the responses due to uncontrolled noisy variables in the experiment. The choice of experimental design for SFE depends on the objectives of the study, investigators' intention, feasibility of experiment, cost-effectiveness, time consumption and many other important factors. For example, to find the most potent factors in a particular experiment, two level factorial designs can be the choice whereas to optimize the previously found influential factors within a predetermined range, more complex designs like Central Composite or Box–Behnken design are appropriate. Based on the objectives of an experiment, all of those designs can be categorized into two broad categories: Screening design and optimization design. Most

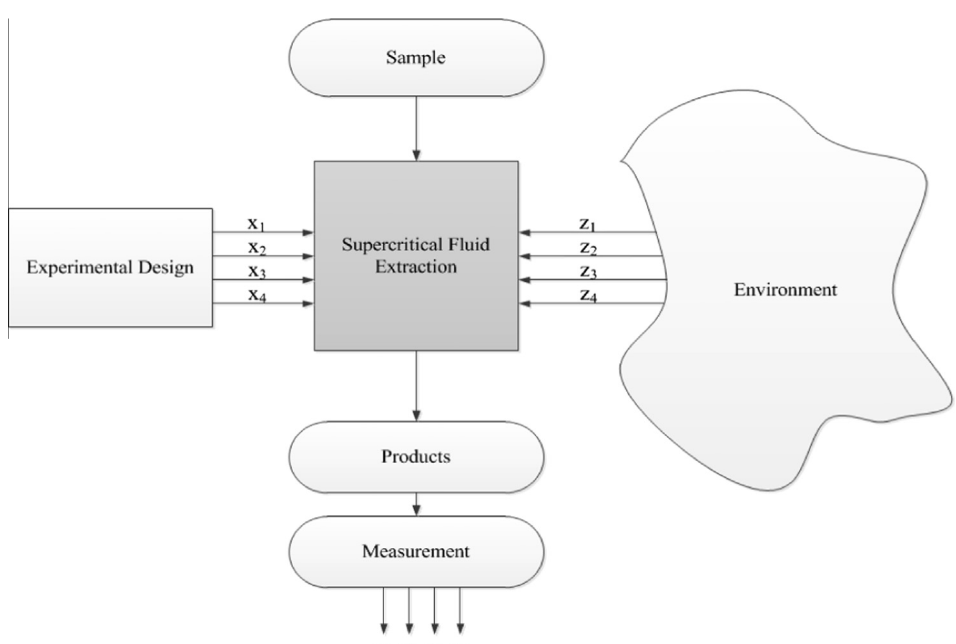

Fig. 1. "Black Box Design" of SFE (adapted from Del Castillo, 2007).