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REVIEW

Recent Development in Counter-current Chromatography

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Abstract: Counter-current chromatography (CCC) is a quick preparative separation technique with immiscible liquid-liquid solvent systems. This paper reviews recent research progress in the instruments improvement of CCC and screening of solvent systems. Moreover, some applications and prospective about chiral resolution by CCC are discussed. Finally, the content and goal of further research in this field are also presented.

Key Words: Counter-current chromatography; Instruments improvement; Solvent systems; Chiral resolution; Review

1 Introduction

In the 1970s, counter-current chromatography (CCC) was invented by Ito on the basis of counter-current distribution. CCC relies on the partition of the solutes between the two immiscible solvent phases. With more than 40 years development, CCC has been used as a semi-preparative and preparative technology for the separation of complex products such as natural products[1–10], proteins[11–15] and nanoparticles[16], *etc*. Compared with other traditional chromatographic separation technology based on the solid matrix support, CCC possesses the special advantages, for instance, it could effectively eliminate the irreversible adsorption and reduce the loss of sample[17].

In this review, we mainly focus on the progress of the improvement of the instrument and the screening of solvent system in recent 5 years, and also introduce the application and prospective of chiral separation by CCC.

2 Instrumentation

With many years accumulative development, preparative and semi-preparative CCC have achieved marked progress in three aspects as (1) Geometric architectures of chromatographic column, (2) Tandem and multiple design of chromatographic column, and (3) Coupling technique between CCC and high performance liquid chromatography (HPLC).

Many systematic works have been carried out around these parts. Aiming to improve the separation efficiency and reduce operating time, diverse functional CCC instruments have been developed and established. Most works are focused on optimizing design of the column to improve retention of the stationary phase, which is a critical parameter in CCC separation. The higher the solid phase retention, the better the peak resolution is obtained. However, the retention of the stationary phase of the traditional CCC was lower than 40%. To improve the retention of the stationary phase, some novel CCC columns have been developed for the separation of complex samples.

A novel conical coil CCC, composed of three identical upright tapered holders in head-to-tail and left-handed direction and connected in series (Fig.1), was built by Wu and his co-workers[18]. The CCC had higher solid phase retention (71.56%). This improvement made it to be a powerful separation tool with high throughput. Cao *et al*[19] developed a spiral tube plate column for the separation of polar compounds. Compared with the traditional CCC, the solid phase retention could increase by 10%. Results indicate that it is an ideal pathway via the optimization of CCC column.

In recent years, people have taken some efforts on tandem and multiple design of chromatographic column. High-speed counter-current chromatography (HSCCC) is based on a variable gravity field produced by two-axis rotation

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mechanism (like planetary motion)[20–24]. However, being limited to its motion model, HSCCC is not suitable for the separation of polar compounds, such as polypeptide, protein and polysaccharide.

Shinomiya *et al*[25] fabricated a novel HSCCC, called coil satellite centrifuge (SCS). The satellite motion was that the coiled column simultaneously rotated around the sun axis, the planet axis and the satellite axis (Fig.2). Compared with traditional CCC with satellite motion, it could obtain a higher retention of solid stationary phase to polar solvent systems. The apparatus was successfully examined in the separation of five sugar derivatives with organic-aqueous two-phase solvent systems at lower speeds.

Besides, a universal CCC with four column holders symmetrically around the rotary frame was built by the same group[26]. The apparatus combined two different planetary motions together: type-J planetary motion and type-I planetary motion (Fig.3). The separation efficiency was compared with two different planetary motions for the separation of same compounds. The experimental results indicated that the universal CCC contained the comprehensive advantages as the two different planetary motions.

Furthermore, some research groups focused on the point of interface with multi-dimensional chromatography. Qiu and his co-workers[27,28] developed two-dimensional CCC × HPLC with heart-cutting techniques (Fig.4). In their work, the 1st CCC

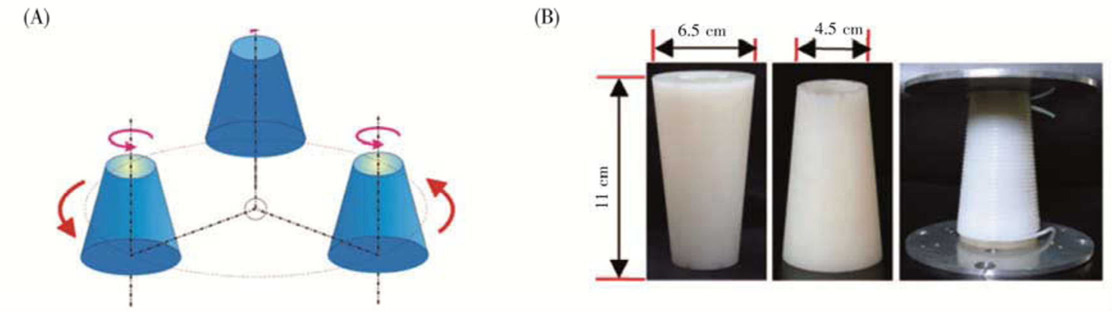

Fig.1 (A) Schematic illustration of the upright conical coils and (B) photographs of the product[18]

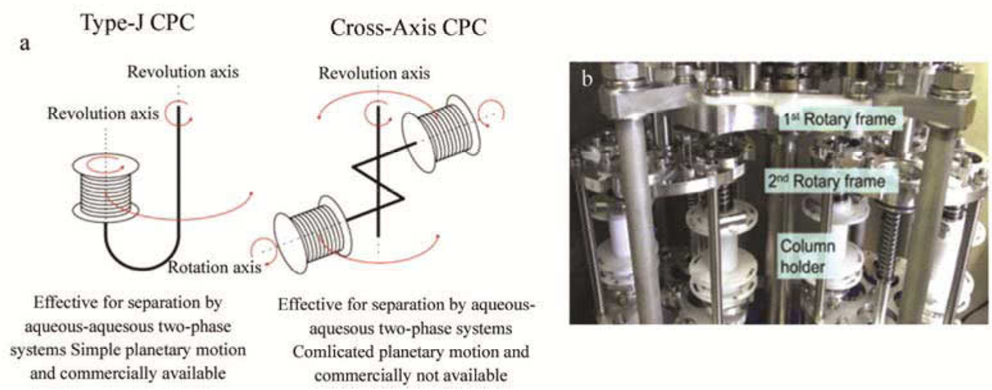

Fig.2 (A) Schematic illustration of planetary motions of type-J coil planet centrifuge (CPC) and cross-axis CPC and (B) photograph of the product[25]

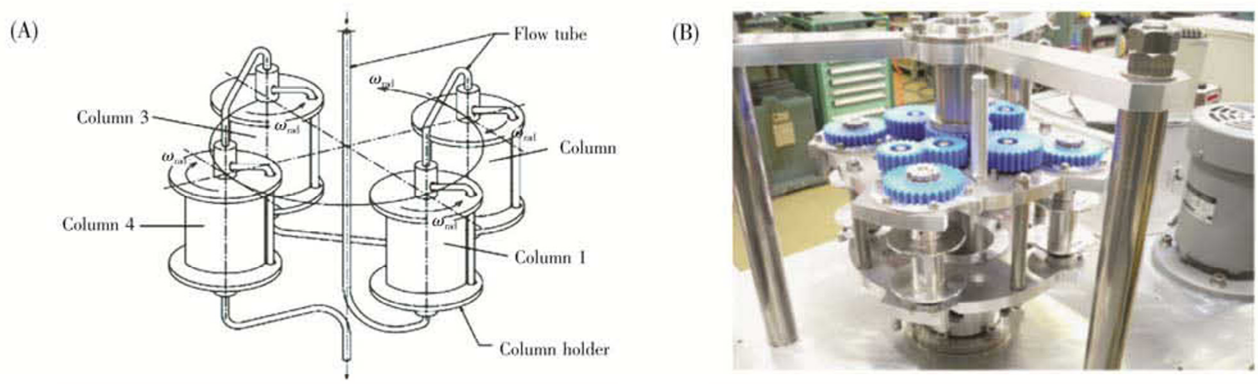

Fig.3 (A) Schematic illustration of type-J forward and the type-I backward columns and (B) photograph of the product[26]