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Review

Solubility of organometallic complexes in supercritical carbon dioxide: A review

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ABSTRACT

The solubility and solubility trends of organometallic complexes in supercritical carbon dioxide are reviewed. The influence of intermolecular forces, physical properties and the metal chelates on solubility is explored. A number of thermodynamic models used to predict the solubility behavior of organometallic complexes in supercritical carbon dioxide, and the advantages and limitations to these thermodynamic models are also discussed.

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1. Introduction

A substance above its critical temperature and pressure is known as a supercritical fluid (SCF). Supercritical fluids exist in a single homogenous phase where the liquid and gas phases are indistinguishable. As such, SCFs have characteristics that are intermediate to those of gases and liquids. Typically, a liquid substance is changed to its gaseous phase by moving it through the vaporization curve, given by path A–B–C in Fig. 1. This involves heating and/or decompression which is accompanied by drastic or abrupt changes to its physical properties. A meniscus is observed as A is changed to C through B. However, a liquid can also be changed to its gaseous form without having to go through phase transition. This is carried out by

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manipulating both temperature and pressure changes; allowing the substance to pass through the supercritical region [path A–D–C] where its physical properties are varied continuously.

The two most distinctive traits of a supercritical fluid are its enhanced mass transfer properties compared to liquids and its variable density. The density of a SCF is highly tunable as it is sensitive to changes in temperature and pressure. As density contributes directly to the solvent strength of a given SCF, the solvating power of a SCF is also easily manipulated. The easy manipulation allows for the maneuvering of process designs to facilitate separation, extraction and deposition of compounds. In most cases, the ease of control and the tune-ability of the liquid-like density of SCFs enable the need for toxic organic solvents to be bypassed. The mass transport properties of SCFs are similar to those of conventional gases and add to the desirability of SCF processes, as their gas-like diffusivity and viscosity allow for faster penetration into solid matrices and surfaces. These characteristics facilitate the deposition of compounds into, and the extraction of compounds from, matrices. In addition, the low operating temperatures typical of SCF processes allows for the processing of thermally-labile compounds, while the sterilizing ability of SCFs adds to the advantages of using SCFs in biomedical and pharmaceutical applications.

Carbon dioxide is the most widely used SCF due to its mild critical temperature (31.1 °C) and pressure (7.38 MPa). It is non-flammable, non-toxic, the second least expensive solvent after water, fairly miscible with a wide variety of organic solvents, easy to recover after processing due to high volatility and is considered 'environmentally friendly' as it can be obtained from existing industrial processes without adding to the greenhouse effect [1,2]. Review on the advantages of supercritical fluids as green processing medium can be found in Beckman [2]. Compared to conventional large molecular-sized solvents, CO_2 with its small linear structure diffuses more quickly [1].

Supercritical fluid technologies have garnered the interest and attention of researchers and industries alike since the late 1970s due to their unique properties [3]. These green technologies have been successfully employed in the decaffeination of coffee [3] and the extraction of spices, hops, tobacco, aromas, essential oils, acetone residues from antibiotics and pharmaceuticals from botanicals [4–12]. In recent years, research efforts in SCF technologies have expanded from mere extractions to sterilizations, micronizations, encapsulations and depositions for biomedical, pharmaceutical, chemical, food, energy and agriculture applications. Current research includes fabrication of three-dimensional porous scaffolds for tissue engineering applications [13], preparation of electrocatalysts for membrane fuel cells through supercritical fluid deposition [14], extraction and in-situ chelation of metals from aqueous and waste solutions [15–19], and encapsulation of active pharmaceutical ingredients (APIs) for controlled delivery purposes [20]. Chemical reactions, properties and applications in SCFs are extensively reviewed in the literature and can be obtained from Refs. [3,21–29].

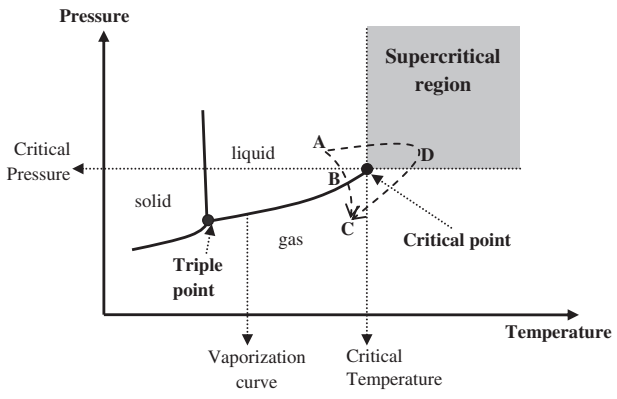

Fig. 1. Phase diagram for a pure substance.

The use of metallic, organometallic and inorganic compounds in chemical and biomedical applications is not new. Metal-based chemotherapeutic drugs such as Cisplatin have been used since the late 1970s and have been proven to be effective in anticancer treatments [30,31]. The success of Cisplatin, or *cis*-diaminedicholoroplatinum(II), has spawned a domino effect on the development of platinum and palladium based anticancer drugs [32–34]. The diverse and varying coordination numbers and structures of organometallics, and the accessible redox states provide many opportunities in the design and application of novel medical therapeutics [35]. Moreover, the intrinsic properties of the cationic metal and ligand allow for control over kinetic and thermodynamic characteristics through ligand design [35–38]. Thus, recent years have seen concerted efforts focused toward the development of metal-based compounds, particularly for diagnostic and therapeutic purposes. Recent developments include the use of ruthenium, yttrium, indium, rhodium, osmium, gold, gallium and cobalt in anticancer therapies [32,39–44] while cyclopentadienyls, arene, carbonyl and carbene are typical classes of ligands used in medicinal therapeutics [36]. Transition metals such as technetium, manganese and iron are also increasingly used in medical imaging as only low dosages are required of these 'highly sensitive materials'. The discovery of molecular targets and the development of nanocarriers carrying metal-based anticancer drugs that selectively target tumors are creating new opportunities for a drug combination therapy where two or more types of therapy (such as chemotherapy and radiotherapy), or two or more APIs, are delivered toward a specific target [45,46]. The use of organometallic compounds in medicinal therapeutics has been reviewed in a number of publications and can be found in Refs. [34,36,47–50].

The significant use of metal-based compounds in imaging, therapeutics and catalysis, and the advantages of SCF technologies have resulted in the initiation of numerous studies of SCF processing of organometallics. These include the deposition of copper films for advanced interconnecting structures using copper(I)(1,1,1,5,5,5,-hexafluoro-2,4-acetylacetonate)(1,5-cyclooctadiene) [51], synthesis of ultra high molecular weight polyethylene (UHMWPE)/silver nanocomposites for total joint replacement components [52], synthesis of gold nanoparticles from gold(I) perfluorooctanoate in supercritical carbon dioxide [53], copolymerization of carbon monoxide and styrene in supercritical CO_2 with palladium complexes as catalysts [54], and the mironization of titanocene dichloride (a metallocene catalyst) via rapid expansion of supercritical solvent (RESS) [55]. However, most SCF related studies on organometallic compounds are heavily concentrated on catalysis and waste metal extractions while research in the area of processing metal-based therapeutics has not received the same level of interest. The exploitations of SCF technologies for homogeneous and heterogeneous catalysis have been reviewed and can be found in Refs. [56–62]. Review on supercritical fluid extraction of metals from aqueous media can be obtained from Refs. [15,63].

While the use of SCFs to process metal-based compounds is gaining ground, a limitation of the technology is a lack of fundamental data. The complexity, the non-ideality and the non-linearity of SCF characteristics make it difficult to predict their behavior and that of the compounds involved under supercritical conditions. The lack of predictability hence, requires extensive, expensive and time-consuming trial and error experimental studies [64]. Phase behavior predictions of solute–SCF systems also become more challenging as the molecular complexity of the solutes increases [65]. While the current thermodynamic models such as the Peng–