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Controlled release of antipyrine from mesoporous carbons

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ABSTRACT

This study investigated the controlled release of a model analgesic drug, antipyrine, from mesoporous carbon, a relatively newer type of drug-delivery medium that is being developed. To synthesize mesoporous carbon a synthetic and a natural precursor, phloroglucinol and lignin, respectively, were employed as carbon sources along with a surfactant, Pluronic F127, as the soft-templating agent that dictates structure. When antipyrine was loaded onto the carbons from its aqueous solution and subsequently allowed to release *in vitro* in simulated gastric fluid, the release was complete within 0.5–3 h (depending on the temperature) for phloroglucinol-derived carbon, whereas 1–7 h was required to complete the release from lignin-derived carbon. The Fickian or molecular diffusion was found to be predominant over Knudsen diffusion and model fitting suggests Fickian diffusivity values of order 10^{-21}–10^{-23} m^2/s. The activation energies for diffusion of antipyrine were found to be 102 and 98 kJ/mol for phloroglucinol and lignin-derived carbons, respectively; the former has higher surface area and pore volume (400 m^2/g and 0.6 cm^3/g) than the later (200 cm^2/g and 0.2 cm^3/g).

1. Introduction

A passive and controlled drug delivery medium is an engineered device that controls the release of a specific loaded drug in a selected physiological system for a sustained interval of time. A smart drug delivery medium is designed in such a way that the release kinetics can be externally influenced by some adequate stimuli (e.g., pH of the release media) in an external magnetic field. Nanoporous media have been utilized quite frequently and successfully for controlled release of drugs [1]. Nearly 40% of the potential drugs are poorly soluble owing to high crystallization energy; therefore, a nanoporous medium provides an intrinsic advantage of being a kinetic inhibitor of crystallization by storing the drugs within its pores in molecularly adsorbed amorphous form. The release of the drug is quite often controlled by resistance in molecular diffusion from pores to the release media that inherently maintains its controlled release. The other associated advantage of a porous-media-based oral drug delivery system can be attributed to its (a) low bulk density, which allows it to float in the gastrointestinal system, and (b) ability to adhere to selective biological systems and offer a volumetric reservoir of drugs [2].

Mesoporous silica of different types such as MCM-41, MCM-48, and SBA-15 were quite frequently employed as controlled drug release media in the past [3]. A large number of model drugs were successfully used to examine the release kinetics of silica-based mesoporous materials for both *in vitro* and *in vivo* experiments; typical examples include antipyrine [4], alendronate [5], amoxicillin [6], captopril [7], erythromycin [8], furosemide, griseofulvin [4], gentamicin [9,10], ibuprofen [11–14], naproxen [15], nimodipine [16], ranitidine hydrochloride [4], sertraline [17], taxol [18], and vancomycin [19]. Despite being used quite frequently as drug release media, silica-based materials possess few inherent difficulties, including weakening of physiological immune systems [20,21], structural instability owing to hydrolysis of siloxane bridges [22,23], and associated cytotoxicity of crystalline silica giving rise to increased granulation in the pulmonary and tracheobronchial lymph nodes [20,21,24,25]. Apart from mesoporous silica, different varieties of metal–organic frameworks (MOFs) were also investigated for their drug release capability [26]. For example, MIL-53 (Cr and Fe) and a few iron- and ruthenium-based MOFs were employed for the release of ibuprofen and a few antitumoral and retroviral drugs [27–29]. However, the key drawbacks associated with MOFs are the gradual leaching of toxic metals to the release medium in the long course of release time, the disintegration of structural entity in acid/basic media, and the expensive nature of almost all MOFs. Although porous silica is well-known for use in drug-delivery, recently carbon nano-materials have been considered for the same purpose [30,31]. Activated carbon can be

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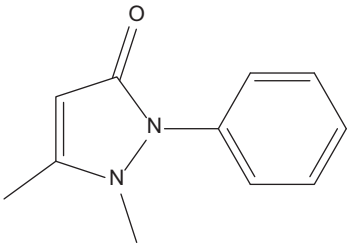

Fig. 1. Chemical structure of antipyrine.

used for adsorptive removal of toxin and employment of porous carbon for medicinal application does not exhibit any evidence of toxicity to human physiology [32]. This encourages us to investigate if mesoporous carbon monolith can be used for adsorption or controlled release of organic molecules.

Our overall goal was to investigate the potential use of nanoporous (mesoporous) carbon as a drug delivery medium. In few earlier studies, mesoporous carbon successfully demonstrated the controlled release of few model drugs [33–40]. Nanoporous carbons are nontoxic [41] and structurally robust monolithic storage media that can be potentially modified to introduce chemical functionality. Although mesoporous carbons have long been synthesized by silica templating, micelle or soft templating has become more popular owing to several difficulties associated with the silica template. In soft templating, a hydroxyl group containing precursor is cross-linked in the presence of a surfactant that forms a self-assembled morphology followed by carbonization of the cross-linked precursor under suitable conditions. The hydrogen bond between the precursor molecules and the surfactant serves as the key driving force to introduce mesoporosity within the generated carbon. Several phenolic precursors such as phenol [42,43], resorcinol [44,45], phloroglucinol [46,47] and hexaphenol [48] have been utilized as the precursor for the mesoporous carbon synthesis. Recently, we have utilized a natural precursor, lignin, to synthesize mesoporous carbons [49]. In this work, we have employed two types of mesoporous carbons derived from a synthetic precursor (phloroglucinol) and natural precursor (lignin). As the pore texture of these two carbons are quite different, it will reflect more light on the role of pore textural properties of mesoporous carbons on drug release mechanism. As mentioned earlier, drug delivery research with mesoporous silica has been reported extensively; whereas, use of mesoporous carbon for the similar

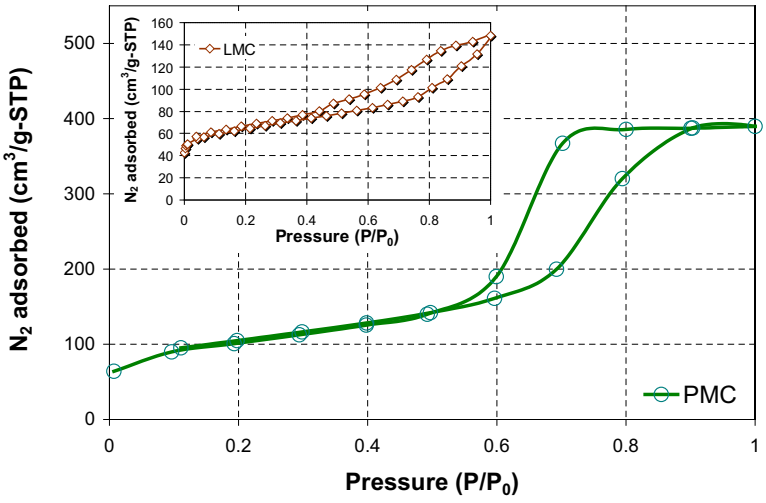

Fig. 2. Nitrogen adsorption–desorption plot of PMC and LMC (*inset*).

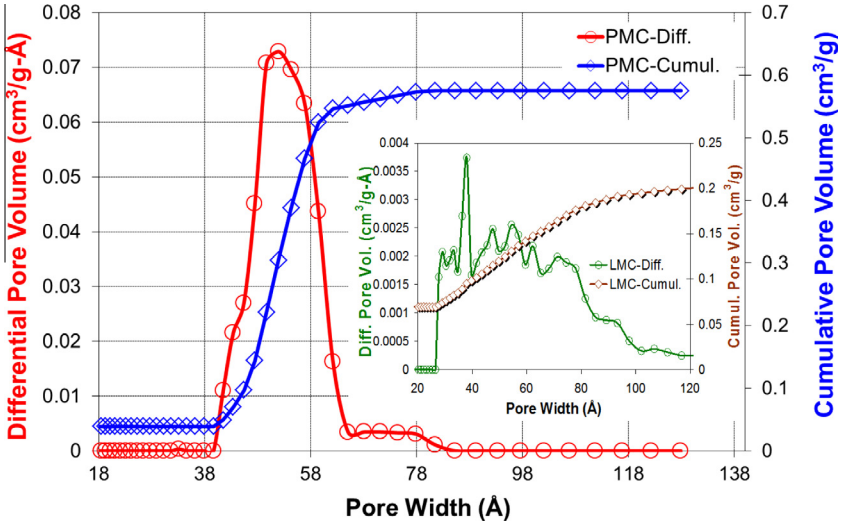

Fig. 3. Pore size distribution of PMC and LMC (*inset*) calculated by nonlocal density functional (NLDFT) theory.