REVIEW OF CLAY-DRUG HYBRID MATERIALS FOR BIOMEDICAL APPLICATIONS: ADMINISTRATION ROUTES

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Abstract—Focus here is placed on the pharmaceutical and biomedical applications of novel clay-drug hybrid materials categorized by methods of administration. Clay minerals have been used for many years as pharmaceutical and medicinal ingredients for therapeutic purposes. A number of studies have attempted to explore clay-drug hybrid materials for biomedical applications with desired functions, such as sustained release, increased solubility, enhanced adsorption, mucoadhesion, biocompatibility, targeting, etc. The present review attempts not only to summarize the state-of-the-art of clay-drug hybrid materials and their advantages, depending on the methods of administration, but also to deal with challenges and future perspectives of clay mineral-based hybrids for biomedical applications.

Key Words—Administration Methods, Biocompatibility, Biomedical Applications, Clay-drug Hybrid, Mucoadhesion, Pharmaceutical Applications, Sustained Release, Targeting.

INTRODUCTION

Much attention has been paid to clay minerals, since the early days of humankind, for various purposes because they are abundant in nature and inexpensive, and because they have unique structural properties (Carretero, 2002; Choy et al., 2007). Clay minerals are, in general, hydrated alumino-silicates containing alkaline and alkaline earth metals. Among the layered clay minerals (phyllosilicates), only some of them, including kaolin, talc (sensu lato), smectites, and fibrous clays can be used as excipients in the formulation of different dosage forms such as solid, liquid, or semisolid. The application of each clay mineral is determined by the individual intrinsic properties derived from the structure type (1:1 or 2:1 layer type) and chemical composition.

The kaolin group of minerals, including kaolinite (Kln) and halloysite, has a 1:1 layer-type structure, in which the layer is composed of a tetrahedral silica sheet and an octahedral alumina sheet combined in a unit, and the layers are stacked along the c axis by hydrogen bonding interaction. Although Kln also has a relatively small specific surface area (SSA) compared to other types of clay minerals, some reports have dealt with its rapid rate of exchange reaction and good adsorption properties on the surface for small molecules such as proteins, bacteria, and viruses (Barral et al., 2008; Rutkai and Kristóf, 2008). Talc (Tlc) is a 2:1 phyllosilicate composed of an edge-linked MgO₄(OH)₂ octahedral sheet located between two corner-linked tetrahedral silica sheets through sharing of oxygen atoms. Talc is an excellent adsorbent due to its large adsorption capacity for hydrophilic and hydrophobic substances (López-Galindo et al., 2007; Rotenberg et al., 2011; Jadhav et al., 2013). Smectite (Sme) is an expandable 2:1 phyllosilicate with a layer charge of −0.2 to −0.6 per formula unit. Each individual layer is composed of a sheet of octahedrally coordinated aluminum, magnesium, or iron atoms with oxygen ligands and hydroxyl groups, which is sandwiched between two sheets of tetrahedral silicons coordinated with oxygen atoms. Smectite is subdivided into dioctahedral and trioctahedral Sme, depending on the number and the nature of octahedral cations. When the octahedrally and/or tetrahedrally coordinated elements are substituted by cations of lower valence such as Mg²⁺ and/or Al³⁺, respectively, a cation exchange capacity (CEC) develops due to the formation of a negative layer charge and its distribution upon substitution. Not only because of its large CEC, surface area, and swellability, but also because of its biocompatibility, Sme has been recommended frequently for biomedical applications, especially pharmaceutics (Gamiz et al., 1992; Aguzzi et al.,...