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# Montmorillonite nanoclay as a multifaceted drug-delivery carrier: A review

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ABSTRACT

Montmorillonite Nanoclay is currently under investigation for its use as a drug carrier system and additive at research level. Being a major fraction of bentonite-a already approved excipient, montmorillonite nanoclay composites are attracting researchers to utilize it in diversed dosage forms, particularly modified release dosage forms. Ability of anionic, cationic and nonionic surfactants to enhance basal spacing to make organoclay are a key feature in efficiency of montmorillonite composites in drug loading and drug release. Factors affecting drug entrapment, molecular level mechanism of interactions, analysis of various reports for sustained drug release and targeted drug release are reviewed for rational selection of montmorillonite in drug delivery. Montmorillonite nanoclay is also efficient to act as a carrier for delivery of therapeutic nucleotide and proteins up to a certain extent. This review is focused on the various aspects of montmorillonite nanoclay such as structure, properties, multifarious applications and biocompatibility studies outcomes.



**Contents**



## 1. Introduction

Montmorillonite, a major constituent of bentonite has been studied for decades for its structural specialties and possibilities to

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make use of the same in pharmaceutical applications. Theories of layer expansion of montmorillonite in the presence of water molecule were already established in the 19th century [1] but the use of such expansion is considered maximum in last two decades. Particularly, nano sized montmorillonite has been successfully used as a drug carrier system [2] solubility enhancer with cyclodextrin [3] use as catalyst in organic synthesis, food additive for prevention of aflatoxicosis [4,5] fabrication of scaffold for biomedical use [6], as adsorbent for nonionic, anionic, cationic dyes and metal ions [7] antibacterial activity in dental infection and in food packaging material [8].

Ease of availability and feasibility of nanosize conversion of particles are two important factors behind interest in this clay mineral. Polymer nanocomposite materials have been used as suitable alternatives to overcome the limitations of micro-composites for drug delivery [9]. Reports of innovative novel techniques like nano-disassembling method, one-pot synthesis [10], microwave assisted technique [11] and injection moulding [12] apart from conventional methods like melt intercalation and various mixing processes in solution state or in colloidal form of preparation of nanocomposites are evident for flexibility of making polymeric nanocomposites including clay materials. Nano form of clay further imparts changes in thermodynamic, chemical and physical properties of the polymer or the composite forming materials. Such altered polymeric blend can be utilized for various drug delivery purposes like, to achieve the desired drug release profile from dosage form, to achieve high drug loading in composites, to enhance stability of entrapped drug substance from external stimuli and to enhance biodegradability of polymers. Key investigations mentioning the use of montmorillonite nanoclay (MMT) for drug delivery are reviewed in this paper. Rationale of the use of MMT in drug delivery is explored, including, molecular interactions and toxicity reports on the basis of end results. Diversified drug delivery application and recent advances of MMT in pharamceutical dosage form design is quite captivating and worthwhile as summarized in this review.

## 2. Characteristics of montmorillonite nanoclay relevant to drug delivery

The structural unit of MMT consisting of two tetrahedral sheets which covers one octahedral sheet in between (Fig. 1). This micaceous clay structure hasoxide anions at the tip of the tetrahedral sub units which are oriented towards silicone atoms which are frequently substituted by aluminium, iron and cations. Whereas the octahedral subunits contains aluminium ions which are substituted by silicon ions and surrounded the hydroxyl atoms present at the axial end of tetrahedral planes [13] Montmorillonite $[(Na,Ca)_{0.33}\ (Al,\ Mg)_2(Si_4\ O_{10})(OH)_2 \bullet nH_2O]$ surface is slightly negatively charged because oxide anions dominate the charge balancing anions (Si+4, Al+3, Fe+2, Fe+3,Mg+2) present in the interface and impart as light overall negative charge to the surfaces of the sheets clay minerals [14]. The MMT particles are plate-shaped, typically 1 nm in thickness and 0.2-2microns in diameter.

Montmorillonite has an excellent sorption property and possesses sorption sites available within its inter layer space as well as on the outer surface and edges. Depending on the place of origin, MMT contains variable amounts of sodium and calcium along with water for hydration. Sodium montmorillonite (Na-MMT) hydrates more than calcium montmorillonite (Ca-MMT) and hence Ca-MMT is converted to Na-MMT with view of higher drug loading and drug release during pharmaceutical applications. Delamination is more prominent in Na-MMT compared to Ca-MMT due to higher hydration extent. It leads to nanoclay platelets-individualization and favors exfoliated nanocomposites with polymers or other similar material. Moreover improved aspect ratio and surface area facilitates higher drug loading. The adsorption and drug release properties of surface charge of MMT is also attributed to pH and concentration of ionic species in the dispersing medium. Edge-to-face heterocoagulation and face-to-face homocoagulation of MMT particles are observed depending on acidic and alkaline pH respectively [15–17]. This cluster orientation impacts drug entrapment and drug release under various ionic strength solutions.

Cation exchange capacity (cmol/kg), specific surface area ($m^2/g$) and basal interlayer spacing are maximum for montmorillonite compared to lllite, kaolinite and muscovite type layered silicate [18]. The cation exchange capacity of MMT is also more than two times than the same capacity of halloysite nanotube, a tubular aluminosilicate clay which is being attempted widely for its pharmaceutical use [19–24]. Interlayer spacing of a 0.9–1.2 nm is enough to accommodate different organic compounds in its structure in nanocomposite formation or drug incorporation.

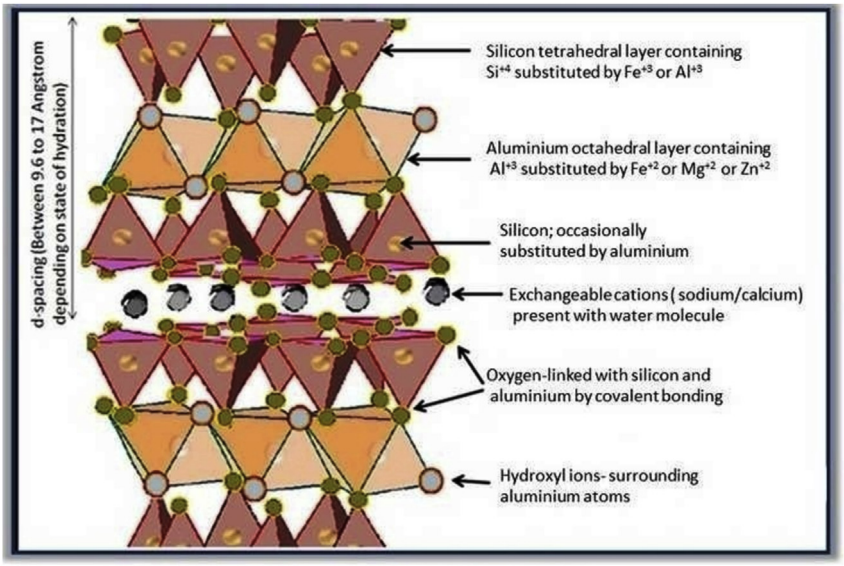


**Fig. 1.** Structural unit of montmorillonite nanoclay.