REVIEW PAPER

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An overview of medical applications of montmorillonite clay

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ABSTRACT

Clays are among the most important material available in nature. Montmorillonite MMT is an important type of clay mineral whose physical structure is typically perceptible as layers and sheets. Each layer is made up of one octahedral and two tetrahedral structural sheets. Due to its distinctive properties, such as swelling and adsorption, MMT has been used in a variety of industrial and therapeutic applications. The high adsorption capacity of MMT contributes to increasing drug intercalation and then its sustained release. By strongly adhering to the drug, MMT typically maintains drug release in many formulations and speeds up the solubility and bioavailability of hydrophobic drugs. MMT has also been used to develop composite delivery systems that combine it with other polymer-based materials. MMT could therefore be used to develop a variety of drug delivery systems to regulate and enhance a drug's pharmacological qualities, such as solubility, dissolution rate, and absorption. An important note to mention is that clays in general are traditionally considered bio-inert or even biocompatible. In this review, the distinguished applications of MMT clay as an agent in the medical field were discussed. Among those applications is its use as an antibacterial agent, detoxification agent, preventive obesity agent, drug carrier agent, and in the treatment of cancer, diarrhea, wounds, and bones.

Introduction

MMT is one of the three-layer clay minerals. The structure of each layer consists of an octahedral sheet sandwiched between two tetrahedral sheets. The silicon-oxygen tetrahedra that make up the tetrahedral sheet are connected by sharing three corners, creating a hexagonal network, while the fourth oxygen atom points downward to the adjacent octahedral sheet. In the aluminum- or magnesium-oxygen-hydroxyl sheet, aluminum or magnesium atoms are octahedrally coordinated to six oxygen or hydroxyl groups, which lie around the metal atom on the six corners of a regular octahedron. The oxygen atoms are shared by neighboring octahedrons, and the hydroxyl groups and oxygen atoms form a hexagonal close packing in two parallel planes, with the metal atoms occupying a central plane (see **Figure 1**).

The unique property of MMT is the ability of water and other polar molecules to enter the unit layers, expanding the basal spacing. The basal spacing varies from 9.6 Å, when there are no polar molecules present in the interlayers, to almost complete separation in some cases [1-5].

MMT clay can be treated with some chemical compounds to improve its surface area and thus increase its adsorption capacity. Among these compounds used are acids such as sulfuric acid [6, 7], hydrochloric acid [8], phosphoric acid [9], and bases such as sodium hydroxide [10]. Other organic and inorganic species can be used for this purpose, such as polysaccharides [11], dodecyltrimethylammonium bromide [12], hexadecyl dimethyl ammonium) chloride [13], octyltrimethylammonium bromide, dodecyltrimethylammonium bromide, cetyltrimethylammonium bromide, and stearyltrimethylammonium bromide [14], zirconium oxide [15]. The adsorption capacity may also be improved with the assistance of microwave and ultrasound [16]. The review aims to summerize the importent application of MMT in the medical feild, focusing on the last ten years.

The subsequent spread of antimicrobial resistance has brought the overuse of antibiotics throughout the years to attention. Certain kinds of microbes can have their growth inhibited or even eliminated by antimicrobial drugs. Several researchers are now particularly interested in finding new products with strong antibacterial action [17-19].

In recent years, varieties of approaches between clay minerals and antibacterial agents have been used to develop clay mineral-based antibacterial complexes. Due to their harmless and eco-friendly features and ease of manufacture through intercalation with organic antibacterial modifiers, clay minerals are being thoroughly investigated [20].

Studies have shown that the antibacterial action of organoclay is due to contact with cells. The activity is further enhanced by the intercalation of polymers with positive charges present on the clay as they nullify the translocation of biocidal cationic surfactant [21]. An antibacterial investigation showed that Co-MMT has

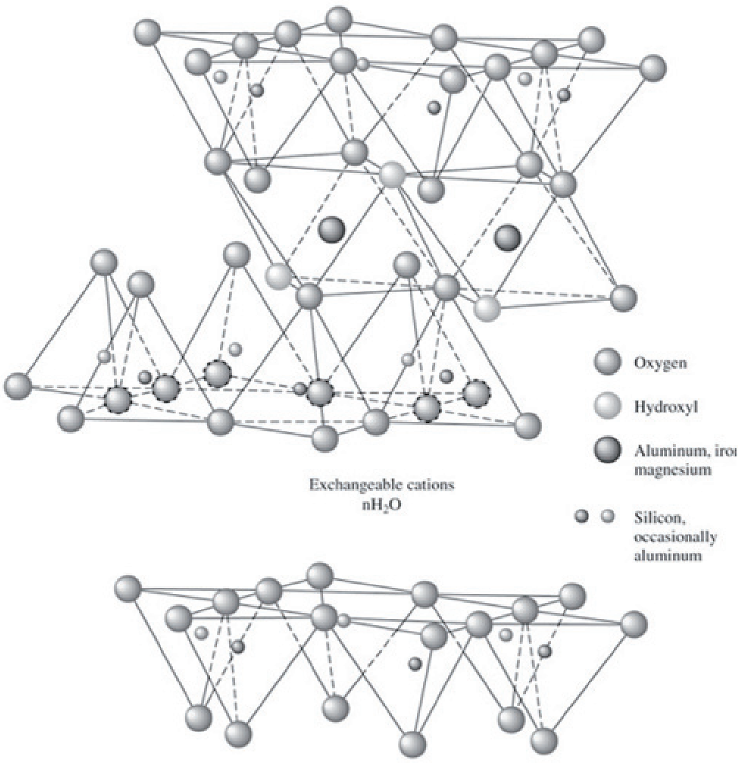

Figure 1. Schematic presentation of MMT antimicrobial application.

good antibacterial activity against *S. aureus* and *E. coli*. These results showed that Co-MMT could be a novel antibacterial agent for tissue engineering due to its superior biocompatibility and antibacterial activity [22]. A study was carried out to evaluate the mechanical characteristics, bonding capabilities, and antimicrobial activity of a new composite cement that contained MMT modified with cetylpyridinium chloride. The composite successfully maintained mechanical strength and bonding performance while achieving continuous anti-biofilm activity [23]. Cetylpyridinium chloride loaded MMT with a long-term antibacterial efficacy to prevent caries was developed as a long-term anti-bacterial agent [24]. A new antimicrobial tissue conditioner including cetylpyridinium chloride and MMT was tested for its mechanical characteristics, antibacterial efficacy, and biocompatibility. Within the limitations of this *in vitro* and *in vivo* study, the findings point to the fact that the newly developed tissue conditioner not only possesses excellent antimicrobial properties but also shares the same mechanical and biocompatibility characteristics as tissue conditioners that are currently on the market [25]. Acanthamoeba keratitis is a painful, potentially dangerous infection of the eye. It frequently tends to be associated with wearing contact lenses. There is a need to develop efficient disinfectants because several lines of evidence point to insufficient contact lens solutions, particularly against the cyst forms of pathogenic acanthamoeba. Cetylpyridinium chloride-MMT was used against keratitis-causing *A. castellanii* belonging to the T4 genotype was investigated. The results indicated that cetylpyridinium chloride-MMT complex has a power antiamoebic effects [26]. A study compares the production of Ag and Cu nanoparticles over MMT nanosheets produced using various reduction media and examines their antibacterial, antifungal, and toxicological activity. The hybrid materials were found to be prospective candidates for next-generation, highly effective antibacterial compounds with lower toxicity [27]. It was observed that a nanocomposite made of bacterial cellulose and silver-modified MMT was effective against Gram-positive *Staphylococcus aureus* and Gram-negative *Pseudomonas aeruginosa* [28]. High-density polyethylene nanocomposite monofilaments based on three different types of metal nanoparticles coated MMT have been the subject of comparative research on their antibacterial properties. In moist environment applications like ropes, sacks, agricultural products, and geotextiles where microbial growth is a concern, the antimicrobial filaments were found to be suitable candidates to replace neat high-density polyethylene counterparts [29]. The effect of MMT and carvacrol (as an antimicrobial agent) on the wettability, mechanical, gas barrier, thermal, and color characteristics of films made from nanoparticles based on methyl cellulose was studied. The mechanical properties of the film material were improved and the melting point of the methyl cellulose film was raised by the addition of MMT to the film matrix [30]. In a study to evaluate the effect of MMT filler on the antibacterial properties of polymer composites with a biodegradable polylactide matrix, the properties of the obtained composites suggest that the MMT may be potentially used as filler for polymer films in the packaging industry [31]. In an investigation on how a vinyl-modified MMT affected the physical and antibacterial qualities of a superabsorbent made of chitosan, graft, and polyacrylic acid, the results obtained encourage the use of the synthesized copolymer nanocomposites in several sectors as better physical antibacterial superabsorbents [32]. To deliver the necessary antibiotic dosages to fight post-implantation infection, a study developed chitosan-MMT nanoclay composites loaded with vancomycin and gentamicin. The results indicated that the prepared composite nanospheres can be a viable choice for preventing bone infections during the post-implantation period [33]. To improve the optical, mechanical, and antibacterial properties of chitosan, MMT-copper oxide nanocomposites were developed using an eco-friendly process. The nanocomposite exhibited strong antibacterial activity against pathogenic *S. aureus* and *B. cereus* and was more effective against these bacteria than it was against *E. coli* and *P. Aeruginosa* [34]. In a study, chitosan-poly(vinylalcohol)-MMT nanocomposites were prepared. The nanocomposites showed poweful antimicrobial properties [35]. A study concerns the potential use of MMT as a carrier and focuses on the intercalation of the clay with the aminoglycoside antibiotic, gentamicin showed the greatest capacity for killing *E. coli* bacteria in an *in vitro* test [36]. MMT clay modified with cetyltrimethyl ammonium bromide was used as a modified layered silicate. The results revealed that the strong nanocomposite antimicrobial activity is due to the interaction between quaternized chitosan and MMT and the fine dispersion of the substance [37]. The antimicrobial activity of organically modified MMT was tested against two Gram-positive bacteria such as *Listeria monocytogenes* and *Staphylococcus aureus* and two Gram-negative ones such as *E. coli* and *Salmonella typhimurium*. The results indicated that the nano MMT caused cell membrane rupture and inactivation of the bacteria [38]. Silver nanoparticles-MMT were synthesized and found to be powerful against a group of Gram-positive and Gram-negative bacteria [39]. Chlorhexidine diacetate and MMT were used in varying amounts to develop organo-MMT. The antibacterial activity against *Escherichia coli* was evaluated and showed promising results [40]. By using electrostatic interaction to enclose a bio-synthesized peptide aptamer with MMT, an antifungal agent was produced. A powerful antifungal activity is shown by the nanocomposite against *Colletotrichum gloeosporioides* [41]. The combination of essential oils with MMT clay produces new materials for various applications including active packaging materials, insecticidal/repellent, antibacterial, and antifungal substances [42]. Silver halides (AgX, X=Cl, Br, I) in MMT were prepared by dispersion method, using silver nitrate as a silver precursor. The product exhibited good antibacterial effects [43].

Detoxification application

MMT clay with layered structures that have large surface areas, which enhances their capacity to bind different compounds on active interlayer surfaces and in pores, can be used as a powerful adsorbent and detoxifier to reduce the bioavailability of the toxic drugs [44].

The potential of MMT clay as an adsorbent for the organochlorine pesticide dieldrin was evaluated. It was found that MMT could be consumed as enterosorbents in the diet to reduce toxin toxicity and bioavailability [45]. Ca-MMT was found to have a high capacity, affinity, and a low therapeutic dose toward polychlorinated biphenyls, the environmental contaminants in food, water, and biota [46]. Ca-MMT was also found to be able to adsorb mixtures of glyphosate and aminomethylphosphonic acid that may reach humans through exposure to contaminated water, soil, and the consumption of crops containing these toxins residues [47]. An investigation demonstrated that MMT modified with Fe, Al, and Ti, has the potential to adsorb deoxynivalenol, which is found in foods and feeds that are contaminated with mildew. It is among the most dangerous mycotoxins, threatening human health as well as animal husbandry [48]. As a mycotoxins adsorbent, octylphenol polyoxyethylene ether modified MMT, a nonionic surfactant, was developed to adsorb polar aflatoxin B1 and weak polar zearalenone, by simulating gastric tract conditions. The surfactant showed the potential to be a useful adsorbent for the simultaneous detoxification of polar and non-polar mycotoxins [49]. Ca-MMT was treated with H_2SO_4, calcination, and organic compounds hexadecyltrimethyl ammonium bromide, cetylpyridinium chloride, and chitosan. The product showed a powerful adsorption performance for mycotoxins [50]. Adsorption role in reducing bioavailability and, consequently, the reported toxicity of monoalkyl trimethyl ammonium salts under environmental circumstances were investigated. The observed toxicity of the compound in the presence of MMT adsorbent was tested on algae. MMT was found to be very effective [51]. The ability of Na-MMT to detoxify two organophosphate pesticides, methyl parathion [O,O-dimethyl O-(p-nitrophenyl) thionophosphate] and tetrachlorvinphos [2-chloro-1-(2,4,5-trichlorophenyl)ethenyl dimethyl phosphate], when treated with N-decyl-N,N-dimethyl-N-(2-aminoethyl) ammonium was found to be adequate [52]. A study focuses on the development of new mycotoxins adsorbents employing zwitterionic surfactants modified MMT for the simultaneous removal of low polar zearalenone and highly polar aflatoxin B1, both of which represent serious health risks. The resulting adsorbent exhibited excellent adsorption performance [53]. An investigation was conducted on Egyptian MMT potential to protect fish from the genotoxicity, histochemical, and biochemical changes caused by aflatoxin B1. It was established that Egyptian MMT could firmly bind aflatoxin in fish guts, hence reducing aflatoxin's bioavailability [54]. The efficacy of Egyptian and Tunisian MMT clays to prevent genotoxicity and histological alterations induced by cadmium chloride using the Nile tilapia fish as an *in vivo* model was investigated. It was found that both clays might tightly bind $CdCl_2$ and reduce its cytotoxicity and genotoxicity, although Tunisian clay was more effective than Egyptian clay [55]. Na-MMT and Ca-MMT were found to be safe and efficacious binders to microcystins [56], and per- and polyfluoroalkyl [57] that can reach humans or animals through the ingestion of food and drinking water that has been contaminated with cyanobacteria. An investigation was performed to assess the ability of MMT to bind uric acid, which increases uric acid diffusion from the blood to the intestine, prevents uric acid absorption in the intestine, and reduces its levels in the blood. The results showed that uric acid could be adsorbed at various doses of MMT in a concentration-dependent manner. The adsorption process moved fast and in acidic solutions, the adsorptive rate was high, whereas, in alkaline solutions, it was low [58]. It was found that MMT considerably adsorbed creatinine in the simulated intestinal solution in a study that intends to assess the adsorption of creatinine by MMT and the acceleration effect of MMT on creatinine excretion from the intestine [59].

Anticancer therapy application

Cancer is a deadly disease that kills people at an alarming rate all around the world. Chemotherapy, radiotherapy, and surgery are all part of the standard cancer treatment [60]. Conventional cancer therapies are often accompanied by undesired side effects. Therefore, the need for alternative anticancer drug delivery agents has become an important medical issue.

A nanocomposite hydrogel drug delivery systems were developed for oral administration based on polyvinyl alcohol and MMT loaded with capecitabine, as an anticancer drug. The developed nanocomposite hydrogel systems for drug delivery showed adequate efficacy against the 4T1 cancer cell line both *in vitro* and *in vivo*, suggesting them viable candidates for the controlled release of anticancer pharmaceuticals in chemotherapy with improved therapeutic benefits [61]. Other researchers reported the formulations of compatible nanocomposite hydrogel films employing carboxymethyl cellulose-hydroxyethyl cellulose-acrylonitrile-linseed oil polyol (CHAP) plain hydrogel and Na-MMT dispersed CHAP nanocomposite hydrogel films. According to the study, the proposed nanocomposite hydrogel films have looked promising for use in therapeutics, particularly for the delivery of anticancer drugs [62]. A novel nanocomposite has been synthesized from MMT as matrix support, nanoparticles of Fe_3O_4 as filler, and carrageenan as a stabilizer. The nanocomposite exhibited good efficacy against cancer cells [63]. Another magnetic nanocomposite with promising anticancer activity was synthesized from MMT as matrix support, Fe_3O_4 as filler, and *Kappaphycus alvarezii* as a stabilizer [64]. MMT, κ-carrageenan, and chitosan were used to synthesize a composite with prolonged cancer therapy and reduced side effects [65]. A study evaluated the intercalation of tamoxifen in Na-MMT interlayer, which is further combined with poly-(ε-caprolactone), for breast cancer oral chemotherapy. The study proved that MMT functions as a drug delivery matrix and also significantly improve delivery proficiency [66]. *In vitro* tests were performed on supramolecular assemblies made from self-assembling MMT nanosheets modified with β-cyclodextrin. The results indicate that the supramolecular assemblies may serve as the basis for the designing of new cancer drug delivery systems [67]. The intercalation of the anticancer drug 5-fluorouracil, in the interlayer of Na-MMT, with the assistance of chitosan produced a significant value in cancer chemotherapy with fewer side effects [68]. MMT nanoparticles were added to chitosan-agarose hydrogel and then loaded with curcumin to prepare a curcumin-loaded nanocomposite hydrogel. The product exhibited good therapeutic effects [69]. The antineoplastic drug, 6-mercaptopurine, was intercalated into Na-MMT interlayer and was further entrapped in poly (L-lactide) matrix to form microcomposite spheres to improve pharmacokinetic proficiency and *in vitro* release and reduce cell toxicity. The produced microcomposite has great potential for anticancer therapy [70].

Diarrhea treatment application

The cause of diarrhea is multiple pathogens and multiple factors, which are primarily brought on by a variety of infections and causes. It is clinically characterized by changes in stool consistency and frequency, and in certain cases, fever, vomiting, and abdominal pain may occur [71].

A typical medicinal substance used to treat pediatric diarrhea is MMT. It can immobilize and inhibit viruses, bacteria, and toxins that may produce in the digestive tract [72]. MMT can reduce stomach pain or discomfort in irritable bowel syndrome patients who experience constipation more frequently [73]. It was observed that giving children with the diarrheal disease a preparation containing MMT, vitamin AD, and zinc could increase short-term efficacy, shorten the time it takes for symptoms to disappear, reduce the level of inflammatory factors, and increase T-lymphocyte levels without raising the incidence of adverse drug reactions. MMT can coat the mucosa of the digestive tract and bind mucosal glycoproteins, repairing and enhancing the mucosal barrier defense against outside influences [74]. The powder of MMT if combined with probiotics could enhance the treatment of diarrhea in children and shorten the time of clinical symptoms, and improve immune function [75]. In addition, the combination of MMT and ZnO was used in reducing diarrhea and enhancing mucosal barrier integrity, and intestinal microflora of weaned pigs [76]. It was also found that the use of berberine in combination with MMT reduced hospitalization time [77]. The duration of acute watery diarrhea can be shortened with MMT and acetorphan [78]. Children's diarrhea can be efficiently reduced with the help of combined zinc gluconate-MMT therapy with no noticeable side effects [79]. In a separate study, it was found that MMT could improve the symptoms of diarrhea and decrease the recovery time of autumn diarrhea in children of different ages [80]. Animal studies have taken an important aspect in this regard. Cu-MMT was found to be as effective in reducing diarrhea and inflammation and improving mucosal barrier integrity and intestinal microflora in weanling pigs [81]. On the other hand, a study suggested that MMT may be a helpful alternative to conventional antibiotics in the treatment and prevention of Salmonella-related animal diarrhea [82].

Obesity prevention application

Being overweight and obese are among the important problems suffered by a large number of people around the world, which have a significant impact on health [83]. Obesity has been linked to several health diseases, including type 2 diabetes, dyslipidemia, nonalcoholic fatty liver disease, cardiovascular problems, and cancer, which are the main causes of death [84-86].

According to recent research, porous colloids including MMT may help prevent weight gain and promote anti-obesity effects [87]. The everyday diet frequently includes fatty foods, and it is generally known that fats play a major role in obesity. Therefore, it is crucial to avoid obesity by immobilizing ingested lipids and raising lipid excretion to lessen fat absorption in the digestive system. MMT as a natural adsorbent clay mineral can adsorb dietary lipids and increase fecal lipid excretion, thus preventing obesity. It was found that MMT crystals can adsorb dietary lipids both *in vitro* and *in vivo*. This ability improves lipid excretion during bowel movements, preventing obesity and its associated comorbidities [88]. Results showed that MMT immobilizes fatty acids and endotoxins via the adsorption-excretion axis in the digestive tract, and MMT could potentially be employed as a prebiotic to prevent intestinal dysbiosis and obesity-associated metabolic problems in obese people [89]. It was also shown that acid-modified MMT can lower lipids by decreasing intestinal absorption and enhancing lipid excretion, so avoiding hyperlipidemia, obesity, and fatty liver [90]. MMT particles with considerable dietary lipid and digestion byproduct adsorptive capabilities were successfully created. These particles might lead to the development of novel, less harmful anti-obesity treatments [91]. According to another research, MMT reduces the dietary lipids and sterols that are absorbed through the gastrointestinal tract, reducing the risk of obesity, hyperlipidemia, and hypercholesterolemia [92].

Wound healing application

Wound healing is a complex and dynamic process that consists of hemostasis, inflammation, proliferation, and remodeling. Different types of cells are involved in this biological process, including neutrophils, macrophages, lymphocytes, keratinocytes, fibroblasts, and endothelial cells [93, 94].

Recent research on nanocomposites made of clay minerals and pharmaceuticals shows that they can interact with biological structures and provide new options for tissue engineering, particularly in the area of wound healing. Due primarily to their potential to reduce water activity, clay minerals may present a variety of opportunities for the development of systems that might facilitate the antimicrobial action of loaded antibacterial drugs, and cell adhesion, growth, and neotissue development [95-98]. Researchers have developed a poly aldehyde dextran MMT composite for controlling large hemorrhages that exhibits excellent tissue adhesion, antimicrobial, and wound healing capabilities [99]. A graphene-MMT composite sponge was also synthesized under a hydrothermal reaction to accelerate wound healing [100]. A nanocomposite made of bacterial cellulose and silver-modified MMT was synthesized as a promising scaffold for healing wounds[101]. To improve wound healing in infected skin lesions, researchers have developed a norfloxacin-MMT nanocomposite as a powder for cutaneous application. The composite appeared to be a useful treatment for burns, diabetic foot ulcers, and other chronic ulcers or skin wounds that are prone to infection [102]. Researchers have also developed electrospun scaffolds, based on biopolymers-MMT intended as a 3D foundation for skin regeneration and repair [103]. To provide a sustained release of chlorhexidine, chitosan-MMT composite films containing chlorhexidine were prepared. All of the produced films demonstrated effective antibacterial wound healing [104]. Using the freezing-thawing method, bionanocomposite hydrogels based on polyvinyl alcohol and egg white as the matrix and MMT nanoclay as the reinforcement were prepared. Clindamycin, an efficient antibiotic, was added to the obtained bionanocomposite hydrogels to provide novel potential wound dressings for treating infected wounds. The bionanocomposite exhibited good effective results concerning infected wounds [105]. Scaffolds were produced from nanocomposites of polycaprolactone and quaternary ammonium salt-modified MMT using the electrospinning technique. The cytotoxicity assessment revealed minimal toxicity and confirmed the efficacy of polycaprolactone-MMT nanocomposite scaffolds as wound dressings [106]. The wound healing property of bacterial cellulose was combined with the antimicrobial activity of MMT to produce novel artificial substitutes for burns. The product showed improved tissue regeneration during wound healing [101]. Nanocomposite hydrogels based on egg white and polyvinyl alcohol and MMT nanoclay were prepared by a facile cyclic freezing-thawing technique. The nanocomposite employed seemed to work well for treating burns and wounds [107]. When combined with a bone-derived polypeptide, the ciprofloxacin-MMT composite demonstrated a promising wound healing progression [108]. As a wound dressing composite, a biopolymer membrane made of chitosan, collagen, and organo-MMT loaded with *Callicarpa nudiflora* was designed. The composite membrane with a porous layered structure exhibited a high swelling ratio, low degradation ratio, and excellent moisture permeability properties [109].

Bone treatment application

With the rise in traffic accidents, there has been a growth in the demand for defective tissues, particularly bone tissues, in recent years. Although autologous bone transplantation remains the best method for treating bone defects, its applicability is somewhat restricted due to its restricted material options, higher surgical trauma, and sensitivity to infection at the bone site [110,111].

MMT is frequently used to reinforce bone scaffolds mechanically [112]. To achieve the nanostrengthening of the composite bone scaffold, it can be converted into graphene-like nanosheets with increased specific surface area through interlayer exfoliation behavior [113]. On the other hand, the MMT crystal structure rich cations between the layers have substantial ion exchange capacity, which can enable intercalation to cause the insertion of ionic polymer molecules into the interlayer areas among its sandwich structure [114]. It is anticipated that employing MMT as the nanofiller phase can significantly improve the mechanical properties of polymer bone scaffolds [115]. By mixing 5 wt% MMT with chitosan solution in an acidic environment, researchers prepared composite materials. They found that the Si-O-Si group of MMT formed hydrogen bonds with the hydroxyl and amino groups of chitosan. The effective transfer of interfacial tension is enhanced by this strong interfacial interaction. As a result, chitosan-MMT has more tensile strength than pure chitosan [116]. Another study found that when the MMT content was less than 4.5 wt%, the tensile strength of the Poly-l-lactic acid/MMT composite increased with the increase of the content and reaches 44.1% [117]. Several studies have been conducted to improve the mechanical properties of MMT intercalated with gelatin and chitosan. It was established that adding MMT made the scaffold pore wall thicker and increased its tensile strength [118]. According to a study on the addition of MMT to nano-hydroxyapatite nanocomposites, adding 10% MMT increased the composite flexural strength and compressive strength by 18.9% and 107.9%, respectively [119]. The effects and mechanism of nano-MMT on osteoblast and osteoclast differentiation were investigated by researchers *in vivo* and *in vitro*. In Ca-deficient ovariectomy rats, the osteogenic effects of high calcium content (3.66 wt%) nano-MMT on alkaline phosphatase activity, mineralization, bone microarchitecture, and expression level of osteoblast and osteoclast associated genes were examined. Nano-MMT was found to attenuate the low-Ca-associated changes in trabecular and cortical bone mineral density. It improved the activity and mineralization of alkaline phosphatase, as well as the expression of genes associated with osteoblast and osteoclast differentiation [120].

Drug carrier application

Drug extended release for patients who require medicinal treatment round the clock is very necessary. MMT generally sustains drug release in various formulations. It also speeds up the absorption and solubility of hydrophobic drugs. To regulate and/or enhance the pharmacological properties of drugs, such as solubility, dissolution rate, and absorption, MMT could be used to develop a variety of drug delivery systems [121].

A study was conducted on the intercalation of timolol maleate into the MMT interlayer at different pH values and concentrations. The drug was successfully intercalated into the interlayer of MMT and its controlled release from MMT-timolol maleate hybrid has been observed during *in vitro* release experiments [122]. Another study was conducted on the preparation and characterization of irinotecan nanocomposite beads based on MMT and sodium alginate as drug carriers. After the incorporation of irinotecan into MMT, the resulting hybrid was compounded with alginate, and irinotecan-MMT-alginate nanocomposite beads were obtained by ionotropic gelation technique. According to the results of the *in vitro* drug release experiments, MMT and MMT in combination with alginate were able to control the release of irinotecan by making it sustained by lowering the released amount and release rate [123]. For topical drug delivery to the eye, MMT and brimonidine (an eye drop to reduce the intraocular pressure) brimonidine-MMT hybridized as a delivery carrier. Via an ion-exchange reaction, the brimonidine molecules were intercalated in the MMT interlayer space to develop the brimonidine-MMT hybrid, which was subsequently combined with polyvinyl alcohol to produce a dry tablet. In *in vitro* conditions, the brimonidine-MMT@polyvinyl alcohol hybrid drug released brimonidine in a sustained manner for more than 5 h. When the hybrid drug was delivered into rabbit eyes *in vivo*, 43% and 18.5% of brimonidine-MMT stayed on the preocular surface for 10 and 60 minutes, respectively. Thus, the brimonidine-MMT@polyvinyl alcohol hybrid drug showed a prolonged decrease in intraocular pressure for 12 h, which was approximately twice as long as that seen with the brimonidine eye drop that is available commercially [124]. A study amid to develop and investigate a drug delivery system formed by intercalation of bromopride with Na-MMT. The results showed that bromoprid was successfully intercalated with the lamellar silicate. In assays, the Na-MMT/bromoprid molecular complex displays a sustained release [125]. A successful one-pot fabrication of ZIF-8-encapsulated medicine is used to develop an MMT-enveloped zeolitic imidazolate framework (M-ZIF-8), which is then followed by MMT coating to produce a core-shell nanoplatform for gastrointestinal (GI) drug delivery. ZIF-8 encapsulated drugs can keep their natural structure, while the MMT layer enhances mucosal adherence and maximizes medicine release. The M-ZIF-8 shows a significant advancement in GI drug delivery [126]. MMT was found to be a suitable material for changing how the tobramycin and norfloxacin drugs are released. The inter-

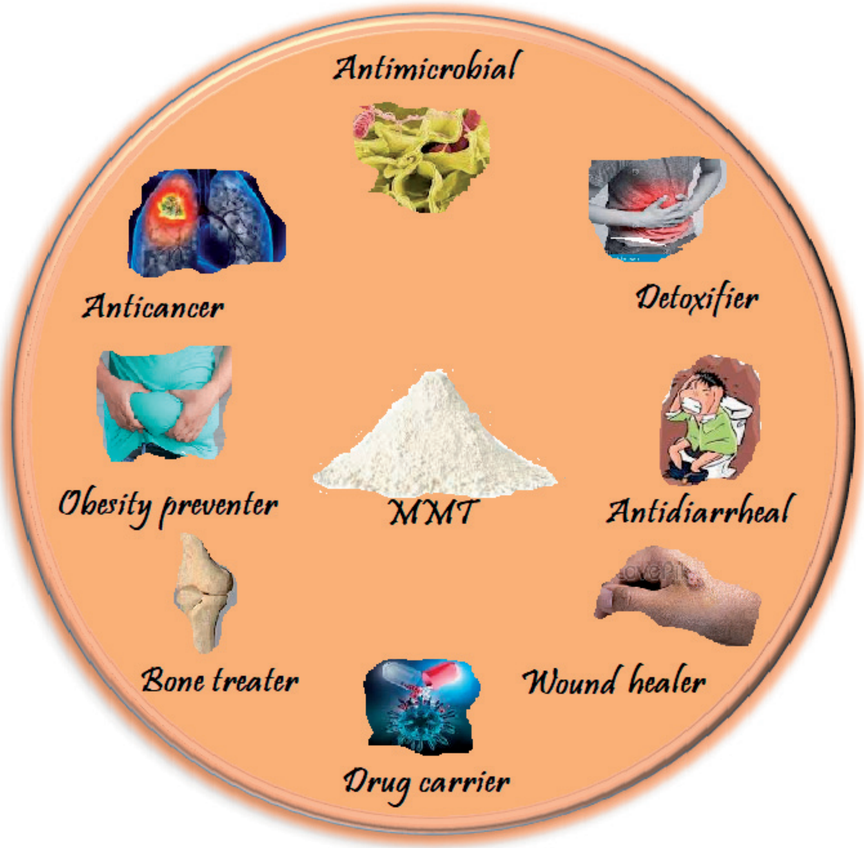

Figure 2. Some of the important medical applications of MMT.

calation of tobramycin or norfloxacin between MMT layers was used to produce drug delivery systems. It was found that the pH of the medium influences the release rates and the percentage of release rises as the pH does [127]. For controlled drug delivery, ring-shaped nanocomposite hydrogel rings made of polyacrylamide, sodium carboxymethyl cellulose, and MMT nanoparticles were developed. The nanocomposite rings were able to prolong release for 15 days in the vaginal fluid simulant, which mimics the vaginal conditions at a pH of 4.2 and a temperature of 37°C. This was demonstrated in an *in vitro* release experiment using methylene blue as a hydrophilic model drug [128]. **Figure 2** summarizes some of the important applications of MMT in the medical field.

Conclusions

MMT is one of the types of clay mineral, which is composed of an octahedral sheet sandwiched between two tetrahedral sheets. This type of clay has received important interest as an additive in polymers and products for enhanced effects. MMT forms composites of different species that can be used in a wide range of therapeutic cases. By significantly adsorbing drug molecules, MMT maintains the release of many pharmaceutical formulations. Pharmaceutical drugs benefit from better drug entrapment and sustained release owing to adsorption capability. The majority of clay mineral investigations focused on how effectively they functioned against toxic substances. There are many important medical applications of MMT such as antimicrobial agents, detoxification agents, cancer therapy agents, preventive obesity agents, as well as treatment of diarrhea and treatment of wounds.

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Conflict of interest statement
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