

Development of Clay Nanoparticles in Pharmaceutical Industry

Shahriyar KARIMDOUST^{1,2*} , Ekrem KALKAN³ , Yalcin Kemal BAYHAN⁴ , Yousef VASIGH⁵ , Beheshteh GHARIBI⁶ 

¹ Department of Geology, Payame Noor University, Ardebil, Iran

² Department of Geology Engineering, Engineering Faculty, Atatürk University, Erzurum, Turkey

³ Department of Civil Engineering, Engineering Faculty, Atatürk University, Erzurum, Turkey

⁴ Department of Environmental Engineering, Engineering Faculty, Atatürk University, Erzurum, Turkey

⁵ Department of Geography, Islamic Azad University, Ardabil Branch, Ardabil, Iran

⁶ Central Laboratory, University of Medical Sciences and Health Services, Ardabil, Iran

*Corresponding author E-mail: karimdoust_sh@yahoo.com

HIGHLIGHTS

- > The properties of mineral-based drugs were examined.
- > The use of nanotechnology in the preparation of therapeutic nano-clays was discussed.
- > Purification and modification of clay minerals to prepare nano-clay was investigated.

ARTICLE INFO

Received : 06 December 2021

Accepted : 28 December 2021

Published : 31 December 2021

Keywords:

Nanotechnology

Nano-clays

Pharmaceutical Industry

Bentonite

ABSTRACT

Nanotechnology has grown significantly in the medical field in recent years. This new technology, with the synthesis and introduction of a new drug system, has made a huge difference in the discussion of treatment and health. The preparation and production of drugs based on natural and mineral compounds and the drug delivery system to specific organs of the body is an example of this technology in the field of pharmacy. Mineral drugs, unlike chemical drugs, have no negative effects on various organs of the body. Nano-clays - with their unique properties - are an example of mineral drugs that play a very important role in the pharmaceutical industry today. Bentonite is a clay mineral that is mainly composed of smectite minerals. Ionic substitution, ductility, high cation exchange are important properties of smectite minerals. Due to the weak bond between the layers in this group, it is easy to add different molecules and polymers between their layers, and for this reason, the clay minerals of the smectite group are very important in the pharmaceutical industry. Scientists are conducting research to purify, modify and optimize bentonite minerals and obtain mineral drugs compatible with the body's biological system.

1. Introduction

In general, clay minerals are hydrated aluminosilicates containing alkaline and alkaline earth metals. Much attention has been paid to them, since the early days of humankind, for various purposes because they are abundant in nature and inexpensive, and because they have unique structural properties [1–3]. Among the layered clay minerals, only some of them, including kaolin, talc, 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 [3].

Clay minerals are a well-known class of compounds that have been used for pharmacological applications since ancient times. They were used for the treatment of minor ailments including infections, pains, aches, and food poisoning in prehistory [1,4]. The medicinal use of clay minerals became more and more prominent when, during the Renaissance, Pharmacopoeia classified clay minerals as

Cite this article: Karimdoust, S.; Kalkan E.; Bayhan Y. K.; Vasigh Y.; Gharibi B. Development of Clay Nanoparticles in Pharmaceutical Industry. *NanoEra* 2021, 2, 54–57



Copyright © 2021 NanoEra.

This is an open access article distributed under the [Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License](https://creativecommons.org/licenses/by-nc-nd/4.0/), which permits unrestricted use, and sharing of this material in any medium, provided the original work is not modified or used for commercial purposes.

drug. Up to now, clay minerals are widely employed in the pharmaceutical industry as common additives. They are for example used as an oral treatment of diarrhea or as gastrointestinal protector; or for topical dermatological applications. Also, they have found application as diluents, lubricants, flavor correctors, carriers of active ingredients in pharmaceutical products, and so on [1,5–9].

Clay nanoparticles attracted much attention in recent years due to their widespread applications are natural materials in nanoscale that originate from clay. The interest in exploiting clay nanoparticles for various purposes is due to their high surface and unique physical and chemical properties [10]. Clay nanoparticles are minerals in clay that have attracted much attention due to the biological application of their abundance in nature, simplicity of construction, and biocompatibility [11–13]. Also, they have a great potential for nutrition because they have been used to treat and protect as a traditional medicine since the beginning of human civilization [14,15]. Clay minerals have been used as laxatives, antidiarrhea, anti-inflammatory agents, blood purification, reducing infections, and healing of stomach ulcers [10,16].

Nanotechnology has grown significantly in recent years, especially in the medical field. This new and valuable technology, with the synthesis and introduction of a new drug system, has taken a huge change and a fundamental step in the discussion of treatment and health. The preparation and production of drugs based on natural and mineral compounds and the drug delivery system to specific organs of the body is an example of the fruit of this technology in the field of pharmacy that has transformed the world of the pharmaceutical industry [17–19] (Fig. 1).

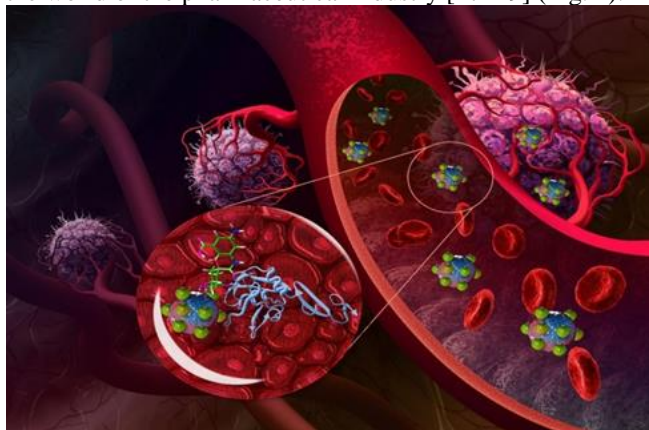


Fig. 1. Nanotechnology for drug delivery applications

The new drug system has no adverse effects on other organs of the body and is compatible with the body's biological environment. Clay minerals are among the most important natural materials used in the preparation and synthesis of drugs of modern pharmaceutical technology. Clay minerals are a group of phyllosilicates or sheet silicates minerals that are very important in the pharmaceutical and nanotechnology industries for various reasons such as abundance, low cost, excellent adsorption properties, etc (Fig. 2). Pharmacists hope to mass-produce this drug to achieve promising results in the treatment of specific and incurable diseases such as cancer [17,20,21].

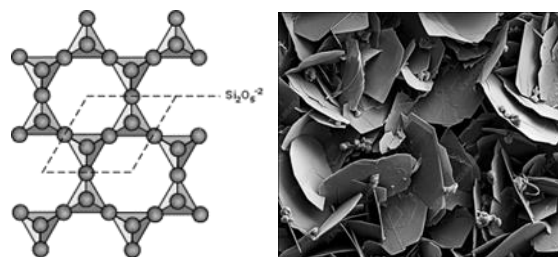


Fig. 2. The Mineral structure of phyllosilicate.

Nano-clays are a group of minerals that are at least one nanometer in size. This group of minerals has attracted the attention of nanotechnology scientists due to its unique properties (Fig.3). By purifying, modifying and optimizing nano-clays, valuable medicinal composites can be obtained that play an important role in health.

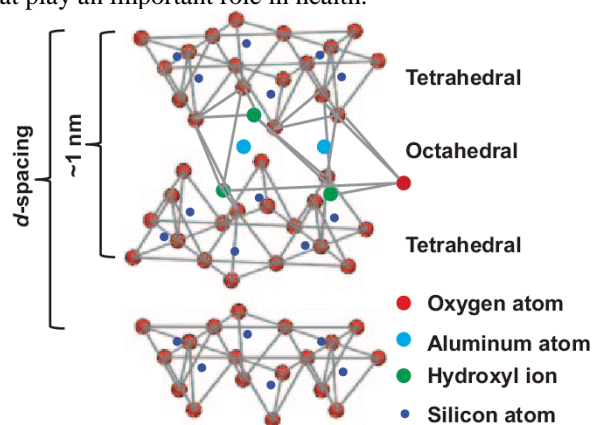


Fig.3. Structure of nano-clay (montmorillonite)

Extensive production of mineral therapists using nanotechnology, which not only has no side effects but also provides minerals needed by various organs of the body, will be an essential step in ensuring human health [20,22].

2. Nano-clays

Clay minerals are inorganic products obtained from the chemical weathering of sedimentary rocks. They have a nanometer-scale layering and are often named just nano-clays [23–28]. The term “nano-clays” is used here to denote clay sand clay minerals whose particles have at least one dimension in the nanoscale range (1-100 nm). The best-known example of a nano-clay is montmorillonite [29–31], a species of the smectite group of hydrous phyllosilicates [23,32].

Nano-clay is composed of thin layers each layer has a thickness of one to a few nanometers' lengths from a few hundred to several thousand nanometers [33]. It consists of silicon-oxygen tetrahedral sheet and aluminum-oxygen octahedral sheet, which are joined to form 1:1 or 2:1 type minerals by sharing the apical oxygens or hydroxyls [34]. Due to the significant presence of clay minerals on earth, people have been collecting this material for thousands of years using them in pottery and medical formulations [25,28,35–37].

3. Results and Discussion

Nano-clays are a group of minerals that are at least one nanometer in size. This group of natural materials has been considered by many nanotechnology scientists due to its special structural properties, cheapness and expansion and

abundance. The advent of nanotechnology, despite its infancy, has been accompanied by major changes in medicine and health. Modification of various properties of materials by changing ions, impregnation with metal elements and treatment with acids in this technology, has provided natural drugs without side effects to the pharmaceutical industry. Bentonite is a clay mineral that is mainly composed of smectite minerals. Ionic substitution, ductility, and high cation exchange are important properties of smectite minerals. Due to the weak bond between the layers, in this group of clay minerals, it is easy to add different molecules and polymers between their layers, and for this reason, the smectite group clay minerals are very important in the pharmaceutical industry [38] (Fig. 4).

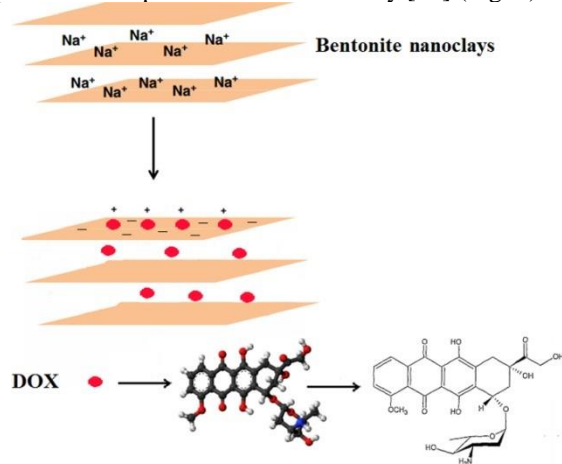


Fig. 4. Addition of effective drugs between cavities and structural spaces of clay mineral layers (bentonite)

The word bentonite was first used in 1898 by a scientist named Knight. The term is derived from the Benton shale area of Wyoming in USA. Bentonite is a clay mineral that is mainly composed of smectite minerals. Smectite consists of dioctahedral series (including montmorillonite, bidlilite, nantronite) and tetrahedral series (including hectorite and saponite clay minerals). The clay structure of the smectite group consists of a layer one nanometer thick. The horizontal dimensions of the layers of these clays vary from 30 nm to several micrometers and depend on the type of silicate [39].

The placement of the layers on top of each other creates a certain space between them, which is known as the interlayer space or the Gallery. Conformal substitution in mineral layers usually results in a negative charge, which is neutralized by alkali or alkaline earth cations (Ca^{+2} , K^+ , Na^+ , ...). The preparation and production of drugs based on natural and mineral compounds and drug delivery system to specific organs of the body is an example of the fruit of this technology in the field of pharmacy that has changed the world of the pharmaceutical industry and has eliminated the damage caused.

Unlike chemical drugs, these mineral drugs do not have any adverse effects on other organs of the body. The addition of effective drugs between cavities and structural spaces of clay mineral layers after refining and modification processes as well as strengthening structural cavities by various physical and chemical methods and finally the preparation of mineral therapeutic nano-fibers is the main method of synthesis of these drugs (Fig. 5).

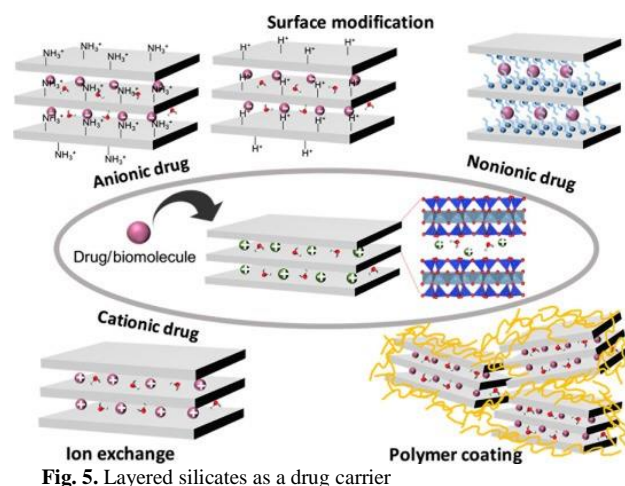


Fig. 5. Layered silicates as a drug carrier

The basic properties of drug carriers (such as nano-clays) are that they protect the drug against degradation, increase its absorption efficiency by facilitating its distribution through the intestinal membrane, and modulate tissue distribution by modulating body function. Also, these mineral drugs do not have any negative or destructive effects on various organs of the body [40].

4. Conclusion

Nano-clays - with their unique properties - are an example of mineral drugs that play a very important role in the pharmaceutical industry today and are one of the most basic nanotechnology tools in the modern pharmaceutical industry. Preparation and production of drugs based on natural and mineral compounds and drug delivery system to specific organs of the body is the product of this technology in the field of pharmacy which has transformed the world of the pharmaceutical industry and eliminated the disadvantages of chemical drugs.

Compliance with Ethical Standards

There is no conflict of interest to disclose.

Conflict of Interest

The author(s) declares no known competing financial interests or personal relationships.

References

- Carretero, M.I. Clay minerals and their beneficial effects upon human health. A review. *Applied Clay Science* **2002**, *21*, 155–163, doi:10.1016/S0169-1317(01)00085-0.
- Choy, J.; Choi, S.; Oh, J.; Park, T. Clay minerals and layered double hydroxides for novel biological applications. *Applied Clay Science* **2007**, *36*, 122–132, doi:10.1016/j.clay.2006.07.007.
- Kim, M.H.; Choi, G.; Elzatahry, A.; Vinu, A.; Choy, Y. Bin; Choy, J.-H. Review of Clay-drug Hybrid Materials for Biomedical Applications: Administration Routes. *Clays and Clay Minerals* **2016**, *64*, 115–130, doi:10.1346/CCMN.2016.0640204.
- Bergaya, F.; Lagaly, G. Chapter 1 General Introduction: Clays, Clay Minerals, and Clay Science 2006, 1–18.
- Carretero, M.I.; Pozo, M. Clay and non-clay minerals in the pharmaceutical industry. *Applied Clay Science* **2009**, *46*, 73–80, doi:10.1016/j.clay.2009.07.017.
- López-Galindo, A.; Viseras, C.; Aguzzi, C.; Cerezo, P.

- Pharmaceutical and Cosmetic Uses of Fibrous Clays 2011, 299–324.
- Carretero, M.I.; Gomes, C.S.F.; Tateo, F. Clays, Drugs, and Human Health 2013, 711–764.
 - Khurana, I.S.; Kaur, S.; Kaur, H.; Khurana, R.K. Multifaceted role of clay minerals in pharmaceuticals. *Future Science OA* **2015**, *1*, FSO6, doi:10.4155/fso.15.6.
 - Massaro, M.; Colletti, C.; Lazzara, G.; Riela, S. The Use of Some Clay Minerals as Natural Resources for Drug Carrier Applications. *Journal of Functional Biomaterials* **2018**, *9*, 58, doi:10.3390/jfb9040058.
 - Mousavi, S.M.; Hashemi, S.A.; Salahi, S.; Hosseini, M.; Amani, A.M.; Babapoor, A. Development of Clay Nanoparticles Toward Bio and Medical Applications. *Current Topics in the Utilization of Clay in Industrial and Medical Applications* 2018, 167–191.
 - Theng, K.G. *The Chemistry of Clay-Organic Reactions*. Adam Hilger Ltd., Rank Precision Ind., 29 King Street, London, WC2E 8JH; 1974; ISBN 0852742118 9780852742112.
 - Nemecz, E. *Clay Minerals*. Budapest, Hungary: Akademiai Kiado; 1981;
 - Chung, H.-E.; Kim, I.-S.; Baek, M.; Yu, J.; Choi, S.-J. Long-term cytotoxicity potential of anionic nanoclays in human cells. *Toxicology and Environmental Health Sciences* **2011**, *3*, 129–133, doi:10.1007/s13530-011-0088-z.
 - Sánchez, C.J.; Parras, J.; Carretero, M.I. The effect of maturation upon the mineralogical and physicochemical properties of illitic-smectitic clays for pelotherapy. *Clay Minerals* **2002**, *37*, 457–463, doi:10.1180/0009855023730045.
 - Veniale, F.; Barberis, E.; Carcangiu, G.; Morandi, N.; Setti, M.; Tamanini, M.; Tessier, D. Formulation of muds for pelotherapy: effects of “maturation” by different mineral waters. *Applied Clay Science* **2004**, *25*, 135–148, doi:10.1016/j.clay.2003.10.002.
 - Gorchakov, V.N.; Dragun, G.N.; Kolmogorov, Y.P.; Smelova, V.A.; Tikhonova, L.I.; Tysjachnova, Y. V The using of SR XRF for estimation of macro- and microelement contents of biological objects at the clay treatment. *Nuclear Instruments and Methods in Physics Research, Section A: Accelerators, Spectrometers, Detectors and Associated Equipment* **2001**, *470*, 437–440, doi:10.1016/S0168-9002(01)01092-0.
 - Carretero, M.I.; Gomes, C.; Tateo, F. *Clays and Human Health*. In: Bergaya, F, Theng, B.K.G., Lagaly, G. (eds.), *Handbook of Clay Science*. Elsevier (The Netherlands); 2006;
 - Murray, H.H. *Applied Clay Mineralogy; Occurrences, Processing and Application of Kaolins, Bentonites, Palygorskite, Sepiolite, and Common Clays*. Elsevier, Amsterdam, The Netherlands; 2007;
 - Karimdoust, S.; Kalkan, E.; Vasigh, Y.; Gharibi, B. Synthesis of Nano-clays-based Drugs, Progression of the Pharmaceutical Industry. , Atatürk University, Nanoscience and Nanoengineering Application and Research Center, 24–26 November 2021, Erzurum, Turkey. In Proceedings of the World Congress on Applied Nanotechnology (W-CAN); 2021.
 - Savjani, K.T.; Gajjar, A.K.; Savjani, J.K. Drug Solubility: Importance and Enhancement Techniques. *ISRN Pharmaceutics* **2012**, *2012*, 1–10, doi:10.5402/2012/195727.
 - Karimdoust, S.; Kalkan, E.; Vasigh, Y.; Ziba, Y.N. The Effect of Nano-clay on Human Gastrointestinal Health. Atatürk University, Nanoscience and Nanoengineering Application and Research Center, 24–26 November 2021, Erzurum, Turkey. In Proceedings of the World Congress on Applied Nanotechnology (W-CAN); 2021.
 - Kaur, M.; Datta, M. Diclofenac Sodium Adsorption onto Montmorillonite: Adsorption Equilibrium Studies and Drug Release Kinetics. *Adsorption Science & Technology* **2014**, *32*, 365–387, doi:10.1260/0263-6174.32.5.365.
 - Floody, M.C.; Theng, B.K.G.; Reyes, P.; Mora, M.L. Natural nanoclays: applications and future trends – a Chilean perspective. *Clay Minerals* **2009**, *44*, 161–176, doi:10.1180/claymin.2009.044.2.161.
 - Kryuchkova, M.; Danilushkina, A.; Lvov, Y.; Fakhruilin, R. Evaluation of toxicity of nanoclays and graphene oxide in vivo: a Paramecium caudatum study. *Environmental Science: Nano* **2016**, *3*, 442–452, doi:10.1039/C5EN00201J.
 - Lazzara, G.; Riela, S.; Fakhruilin, R.F. Clay-based drug-delivery systems: what does the future hold? *Therapeutic Delivery* **2017**, *8*, 633–646, doi:10.4155/tde-2017-0041.
 - Piétrement, O.; Castro-Smirnov, F.A.; Cam, E. Le; Aranda, P.; Ruiz-Hitzky, E.; Lopez, B.S. Sepiolite as a New Nanocarrier for DNA Transfer into Mammalian Cells: Proof of Concept, Issues and Perspectives. *The Chemical Record* **2018**, *18*, 849–857, doi:10.1002/tcr.201700078.
 - Yilmaz, B.; Irmak, E.T.; Turhan, Y.; Doğan, S.; Doğan, M.; Turhan, O. Synthesis, Characterization and Biological Properties of Intercalated Kaolinite Nanoclays: Intercalation and Biocompatibility. *Advances in Materials Science* **2019**, *19*, 83–99, doi:10.2478/adms-2019-0007.
 - Peixoto, D.; Pereira, I.; Pereira-Silva, M.; Veiga, F.; Hamblin, M.R.; Lvov, Y.; Liu, M.; Paiva-Santos, A.C. Emerging role of nanoclays in cancer research, diagnosis, and therapy. *Coordination Chemistry Reviews* **2021**, *440*, 213956, doi:10.1016/j.ccr.2021.213956.
 - Lepoittevin, B.; Devalckenaere, M.; Pantoustier, N.; Alexandre, M.; Kubies, D.; Calberg, C.; Jérôme, R.; Dubois, P. Poly(ϵ -caprolactone)/clay nanocomposites prepared by melt intercalation: mechanical, thermal and rheological properties. *Polymer* **2002**, *43*, 4017–4023, doi:10.1016/S0032-3861(02)00229-X.
 - Jeon, H.S.; Rameshwaram, J.K.; Kim, G.; Weinkauff, D.H. Characterization of polyisoprene–clay nanocomposites prepared by solution blending. *Polymer* **2003**, *44*, 5749–5758, doi:10.1016/S0032-3861(03)00466-X.
 - Wang, K.; Wang, C.; Li, J.; Su, J.; Zhang, Q.; Du, R.; Fu, Q. Effects of clay on phase morphology and mechanical properties in polyamide 6/EPDM-g-MA/organoclay ternary nanocomposites. *Polymer* **2007**, *48*, 2144–2154, doi:10.1016/j.polymer.2007.01.070.
 - Guggenheim, S.; Adams, J.M.; Bain, D.C.; Bergaya, F.; Brigatti, M.F.; Drits, V.A.; Formoso, M.L.L.; Galán, E.; Kogure, T.; Stanjek, H. Summary of recommendations of nomenclature committees relevant to clay mineralogy: report of the Association Internationale pour l’Etude des Argiles (AIPEA) Nomenclature Committee for 2006. *Clay Minerals* **2006**, *41*, 863–877, doi:10.1180/0009855064140225.
 - Bh, S.; M, P.; Vm, B.; Tp, H. Modified nano-clay formulation and their application. ~ 705 ~ *International Journal of Chemical Studies* **2018**, *6*, 705–710.
 - Lu, T.; Gou, H.; Rao, H.; Zhao, G. Recent progress in nanoclay-based Pickering emulsion and applications. *Journal of Environmental Chemical Engineering* **2021**, *9*, 105941, doi:10.1016/j.jece.2021.105941.
 - Zhang, D.; Zhou, C.-H.; Lin, C.-X.; Tong, D.-S.; Yu, W.-H. Synthesis of clay minerals. *Applied Clay Science* **2010**, *50*, 1–11, doi:10.1016/j.clay.2010.06.019.
 - Gaskell, E.E.; Hamilton, A.R. Antimicrobial clay-based materials for wound care. *Future Medicinal Chemistry* **2014**, *6*, 641–655, doi:10.4155/fmc.14.17.
 - Viseras, C.; Carazo, E.; Borrego-Sánchez, A.; García-Villén, F.; Sánchez-Espejo, R.; Cerezo, P.; Aguzzi, C. Clay Minerals in Skin Drug Delivery. *Clays and Clay Minerals* **2019**, *67*, 59–71, doi:10.1007/s42860-018-0003-7.
 - Eisenhour, D.D.; Brown, R.K. Bentonite and Its Impact on Modern Life. *Elements* **2009**, *5*, 83–88, doi:10.2113/gselements.5.2.83.
 - Khediri, F.; Mrad, A.I.; Azzouz, M.; Doughi, H.; Najjar, T.; Mathieux-Fortunet, H.; Garnier, P.; Cortot, A. Efficacy of Diosmectite (Smecta)® in the Treatment of Acute Watery Diarrhoea in Adults: A Multicentre, Randomized, Double-Blind, Placebo-Controlled, Parallel Group Study. *Gastroenterology Research and Practice* **2011**, *2011*, 1–8, doi:10.1155/2011/783196.
 - Baek, M.; Choy, J.-H.; Choi, S.-J. Montmorillonite intercalated with glutathione for antioxidant delivery: Synthesis, characterization, and bioavailability evaluation. *International Journal of Pharmaceutics* **2012**, *425*, 29–34, doi:10.1016/j.ijpharm.2012.01.015.