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Inorganic polymers as drug carriers: opportunities and challenges

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Abstract

Innovative methods and significant developments in designing new synthetic inorganic materials have been used to overcome limitations of current drug delivery systems. Inorganic polymers are widely used in the field of biomedicine, imaging, tissue engineering and drug delivery because of their bioactivity, biocompatibility, and stability. A few of the more well-known wholly inorganic polymers are portland cement, silicon dioxide, polyanionic glasses (including titania- and aluminosilicate glasses), poly(sulphur nitride), polycrystalline diamond, graphite, poly(sulphur nitride), and aluminum-silicate materials. Inorganic polymers, especially those possessing significant porosity, are good potential candidates for the delivery of several drugs (anticancer, antibiotics, and anti-inflammatories), providing advantages such as encapsulation, controlled delivery, and improved targeting of drugs. Choosing a suitable drug carrier with a selective targeting potential also seems to be a very promising way for improving stability as well as selectivity. Despite all the advances, developing homogeneous inorganic polymers with narrow molecular weight distributions is a multidisciplinary challenge. The current keynote speech provides a review of the opportunities and challenges of using inorganic polymers as drug carriers.

KEYWORDS
inorganic polymers, drug delivery, controlled delivery, drug encapsulation, drug carriers

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MAIN MESSAGE

Inorganic polymers comprise a unique classification of polymers containing only inorganic atoms in their main chain, and have wide applications. The number and variety of elements as well as the tailoring of new structures of these polymers can offer them unique size- and shape-dependent physicochemical properties, high thermal stability due to strong bond formations, and high loading capacities; these properties along with the high abundance of inorganic materials in the earth's crust, are the main reasons to attend inorganic polymers as special materials with unique properties. Additionally, these structures can also be conjugated with targeting agents to improve their therapeutic effects. The different set of applications of inorganic polymers are: (i) tumour targeting, photothermal therapy, and immunotherapy mediators,

(ii) imaging agents [1], and (iii) the delivery of bioactive molecules such as drugs [2,3], genetic material, *etc*.

Polysiloxanes, polysilanes, polyphosphazenes, polyoxometalates, zeolites, other aluminum-silicates (including natural minerals and industrial wastes like kaolin, fly-ash, and slag from blast furnace), and polymeric carbons (such as diamonds and graphite) are some examples of inorganic polymers. Herein, the opportunities and challenges of using these polymers as drug delivery systems are discussed.

Polysiloxane and polysilane due to their biocompatibility, stability, optical transparency, and low toxicity are broadly used in the production of biomedical devices. Although, the hydrophobic structure of these types of polymers can be used as a hydrophobic drug carrier for molecules such as nifedipine or ibuprofen, this property barricades their application in drug delivery systems (such as those involving cell adhesion, long-term cell culture, or surgical implants). Moreover, they can be easily contaminated by pathogens and proteins. In order to improve hydrophilicity in these types of inorganic polymers, the functionalization of their surface has been attempted by using several physical and chemical treatments.

Polyphosphazenes with a phosphorus-nitrogen backbone, due to their biological performance, biocompatibility, and degradability, are used for antimicrobial and anticancer agents, drug and gene delivery, vaccine immunoadjuvants, and tissue engineering. It is known that macromolecules can selectively accumulate in malignant tissues due to a phenomenon known as the “enhanced permeation and retention effect” (“EPR effect”) [4]. This happens because the uncontrolled growth of tumours makes them permeable to macromolecules, due to defects on the surrounding vascular and lymphatic structures. Therefore, the selective targeting of tumours and cancer cells might be achieved by using several formulations of functionalized phosphazene.

Polyoxometalates (POMs) have been considered as novel, low-cost, transition metal oxide, nanosized inorganic drugs with anticancer, antibacterial, and antiviral properties [5]. Recently, POMs were found to be promising anticancer drug candidates [6]. Despite the advantages of using purely inorganic POMs, these compounds mostly suffer from side-effects like high and long-term toxicity, thereby impeding their clinical application. Therefore, the functionalization and encapsulation of POMs with organic moieties in order to synthesize modified organic-inorganic hybrids can not only reduce the toxicity of the POMs, but also increase their potential as chemotherapeutic agents.

The tunable structures, various pore sizes, chemical stability, high loading efficacy, and biocompatibility of zeolites make them attractive as drug delivery systems. The ion exchange capacity of zeolites is the most desirable function of a drug release mechanism. Various zeolites have been used as drug carriers for ibuprofen, 5-fluorouracil, diclofenac sodium, aspirin, doxorubicin hydrochloride, indomethacin, and levofloxacin. Despite the numerous advantages of zeolites as drug delivery systems, drug molecules can be released rapidly from the large pore size of zeolites, which is a serious challenge. Therefore, the modification of the zeolite is necessary so as to achieve a controlled release profile of the loaded drug [7].

Finally, nano-diamond-based drug delivery systems are excellent hydrophilic and hydrophobic drug carriers that can release drugs in response to light, pH, temperature, or enzymes. However, the major concern of nano-diamond carriers as drug delivery systems is their significant toxicity. In addition, they are characterized by a highly oxidized surface and carry numerous functional groups that directly affect the stability and agglomeration of nano-diamonds in a variety of media. Hence, mechanical and chemical surface modifications are used in order to reduce agglomeration and to enhance the stability and solubility in a variety of polar organic solvents, by substituting the functional groups on their surface [8].

Inorganic polymers are widely used in the field of biomedicine due to their biocompatibility, bioactivity, and stability; however, their use is limited by their nonspecific distribution throughout the body, leading to high doses, poor pharmacokinetics, rapid clearance, and major side-effects [9].

CONFLICT OF INTEREST STATEMENT

The author declares no conflicts of interest.

REFERENCES

1. Atashi Z., Divband B., Keshtkar A., Khatamian M., Farahmand-Zahed F., Nazarlo A.K., *et al.*: Synthesis of cytocompatible Fe_3O_4@ZSM-5 nanocomposite as magnetic resonance imaging contrast agent. *J. Magn. Magn. Mater*. 438: 46-51 (2017).
DOI: **10.1016/j.jmmm.2017.04.062**

2. Karimi M., Habibizadeh M., Rostamizadeh K., Khatamian M., Divband B.: Preparation and characterization of nanocomposites based on different zeolite frameworks as carriers for anticancer drug: zeolite Y *versus* ZSM-5. *Polym. Bull*. 76: 2233-2252 (2019).
DOI: **10.1007/s00289-018-2472-1**

3. Sayed E., Haj-Ahmad R., Ruparelia K., Arshad M.S., Chang M.W., Ahmad Z.: Porous inorganic drug delivery

systems - a review. *AAPS PharmSciTech* 18(5): 1507-1525 (2017).
DOI: **10.1208/s12249-017-0740-2**
PMID: **28247293**

4. Matsumura Y., Maeda H.: A new concept for macromolecular therapeutics in cancer chemotherapy: mechanism of tumoritropic accumulation of proteins and the antitumor agent smancs. *Cancer Res*. 46(12 Pt 1): 6387-6392 (1986).
PMID: **2946403**

5. Karimian D., Yadollahi B., Mirkhani V.: Dual functional hybrid-polyoxometalate as a new approach for multidrug delivery. *Microporous Mesoporous Mater*. 247: 23-30 (2017).
DOI: **10.1016/j.micromeso.2017.03.048**

6. Bijelic A., Aureliano M., Rompel A.: Polyoxometalates as potential next-generation metallodrugs in the combat against cancer. *Angew. Chem. Int. Ed. Engl*. 58(10): 2980-2999 (2019).
DOI: **10.1002/anie.201803868**
PMID: **29893459**

7. Khatamian M., Divband B., Farahmand-Zahed F.: Synthesis and characterization of Zinc (II)-loaded zeolite/graphene oxide nanocomposite as a new drug carrier. *Mater. Sci. Eng. C Mater. Biol. Appl*. 66: 251-258 (2016).
DOI: **10.1016/j.msec.2016.04.090**
PMID: **27207061**

8. Chauhan S., Jain N., Nagaich U.: Nanodiamonds with powerful ability for drug delivery and biomedical applications: recent updates on *in vivo* study and patents. J*. Pharm. Anal*. 10(1): 1-12 (2020).
DOI: **10.1016/j.jpha.2019.09.003**
PMID: **32123595**

9. Valente A., Precker R.L.M., Hey-Hawkins E.: Inorganic polymers for potential medicinal applications. In: Hey-Hawkins E., Hissler M. (editors): Smart Inorganic Polymers: Synthesis, Properties, and Emerging Applications in Materials and Life Sciences. Weinheim: Wiley-VCH, 243-276 (2019).