Diamondoids – The Molecular Lego of Biomedicine, Materials Science and Nanotechnology

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A Brief Description of Diamondoids

Diamondoids are a peculiar class of organic molecules with unique structures and properties. Diamondoid molecules (AKA polymantanes, adamantologs) are cage-like, ultra stable, saturated hydrocarbons. The basic repetitive unit of diamondoids is a ten-carbon tetracyclic cage system called “adamantane” (Figure 1a). Adamantane consists of cyclohexane rings in ‘chair’ conformation. These molecules are called “diamondoids” because their carbon-carbon framework is completely, or largely, superimposable on the diamond lattice (Figure 2). Diamondoids show unique properties due to their exceptional atomic arrangements. The discovery of adamantane cage in 1933 [1] and its direct synthesis in 1957 [2] has turned this diamondoid and its derivatives into readily available compounds with numerous applications. Since 1960, the interest in practical applications of diamondoid molecules has steadily increased [3]. Diamondoids are presently molecular building blocks for biomedicine, materials science and nanotechnology that enable the design and manufacturing of nanometer-scale structures programmed to have virtually any desired shape and properties [4-6].

Diamondoids were first discovered in petroleum [1] and since there has been limited progress in synthesizing them there have been continuous efforts in exploring them in petroleum and other fossil fuels [7-10]. The presence of diamondoids in fossil fuels has become much more than a chemical curiosity and has advanced to be a resourceful template and molecular building blocks in nanotechnology such as molecular self-assembly (Figure 4), in design of NEMS and MEMS, in nanodrug delivery and targeting, in DNA-directed assembly nannstructure formation (Figure 5), and in host-guest chemistry. Diamondoids have very high melting points as compared with other hydrocarbons and organic molecules. Diamondoids have negative electron affinities and they are transparent to visible light and high electrical insulating properties as diamond. Since diamondoids

Figure 1: Molecular structures of lower diamondoids: (a): Adamantane (b): Diamantane (c): Triamantane (d): Anti- isomer of Tetramantane.

Figure 2: Structures of adamantane, diamantane and triamantane superimposed over the three-dimensional diamond network.
Mycobacterium tuberculosis

In conclusion, and they are used as drugs for diabetes treatments. A number of adamantane derivatives possess hypoglycemic action. Derivatives is an additional important application of these substances. Design some other diamondoids derivatives for Alzheimer’s disease is another important set of biomedical applications of these compounds. Designing molecular capsules, designing new antidotes to counteract the effect of a poison by diamondoid molecules, which is present in all adamantane derivatives, might be responsible for their ability to penetrate into the blood-brain barrier. Adamantane nucleus, especially for the fact that due to their lipophilicity / hydrophobicity they can easily pass through blood-brain barrier. Adamantane derivatives in drug delivery and drug targeting, especially for the fact that due to their lipophilicity / hydrophobicity they can easily pass through blood-brain barrier. Adamantane nucleus, which is present in all adamantane derivatives, might be responsible for their ability to penetrate into the blood-brain barrier (BBB) and their accumulation in the CNS. Their applications for pharmacophore-based drug design, for drug delivery and drug targeting systems is a new matter of considerable importance.

Biomedical Applications of Diamondoids and Derivatives

There have been great research interest and activities in understanding how diamondoid molecules interact with living systems, how these interactions could be useful in their biomedical applications, and characteristics of these molecules as tools for diagnosis and cell metabolism screening.

Among all diamondoids, adamantane and its derivatives have been most widely used for drug design. Starting from the late 50’s and early 60’s, the hydrophobic nature associated with the compact and highly symmetrical structure of the adamantane molecule have attracted researches interested in the discovery of structurally unprecedented drugs, such as polyhaloadamantane pesticides; and new or improved biological activities conferred by a caged moiety attached to known bioactive substances, such as orally active hypoglycemic sulfonylureas. It is also known that adamantly group changes the properties of known drugs or provides an important pharmacophore for the design of new drugs.

Diamondoid derivatives in drug delivery and drug targeting, especially for the fact that due to their lipophilicity / hydrophobicity they can easily pass through blood-brain barrier. Adamantane nucleus, which is present in all adamantane derivatives, might be responsible for their ability to penetrate into the blood-brain barrier (BBB) and their accumulation in the CNS. Their applications for pharmacophore-based drug design, for drug delivery and drug targeting systems is a new matter of considerable importance.

Already diamondoids are used to design drugs in fighting infectious diseases like Influenza Viruses and HIV, bacterial infections like Gram-positive bacteria and MTR (Mycobacterium tuberculosis), and parasitic infection treatments like antimalarial drugs. Fighting cancer with diamondoids derivatives is another important application of these interesting compounds. Among such derivatives adaphostin is a prodrug retinoid derivative, is used for chemotherapy and exert selective antiproliferative and cytodifferentiating effects. These actions are of special interest in the search for new antineoplasic agents. Neuroprotective effect of memantine (a derivative of asamantane) and its analogs is used for chemotherapy and exert selective antiproliferative and cytodifferentiating effects. These actions are of special interest in the search for new antineoplasic agents.

Table 1: Major Applications of Diamondoids and Derivatives.

| Applications                                                                 |
|------------------------------------------------------------------------------|
| Antiviral drug                                                                |
| Cages for drug delivery                                                      |
| Crystal engineering                                                          |
| Designing molecular capsules                                                 |
| Design of new antidotes                                                      |
| Diamondoid-DNA nanoarchitectures                                             |
| Drug delivery (they can easily pass through blood-brain barrier due to their lipophilicity / hydrophobicity) |
| Drug targeting                                                               |
| Fighting infectious viral diseases (influenza etc.)                          |
| Fighting infectious bacterial diseases (tuberculosis, etc.)                   |
| Fighting infectious parasitic diseases (malaria, etc.)                       |
| Fighting cancer (new antineoplasic agents)                                   |
| Gene delivery                                                                |
| Hypoglycemic action (drugs for diabetes treatment, etc.)                     |
| In designing an artificial red blood cell, called Respirocyte                |
| In host-guest chemistry and combinatorial chemistry                          |
| MEMS                                                                         |
| Molecular machines                                                           |
| Molecular probe                                                              |
| Nanodevices                                                                  |
| Nanorobotics                                                                 |
| Nanofabrication                                                              |
| Nanocomposites                                                               |
| Nanomodule                                                                   |
| NEMS                                                                         |
| Neuroprotective effect (for Alzheimer’s disease, etc.)                       |
| Organic MBBs in formation of nanostructures                                  |
| Pharmacophore-based drug design                                              |
| Polymer, co-polymers                                                         |
| Positional assembly                                                          |
| Power cells overcharge protecting compounds                                  |
| Preparation of fluorescent molecular probes                                  |
| Prodrugs                                                                     |
| Rational design of multifunctional drug systems and drug carriers            |
| Self-assembly: DNA directed self-assembly, host-guest chemistry              |
| Shape-targeted nanostructures                                                |
| Synthesis of supramolecules with manipulated architecture                    |
| The only semiconductors which show a negative electron affinity              |
| Microelectronics (thermally conductive films in integrated circuit packaging, low-k dielectric layers in integrated circuit multilevel interconnects, thermally conductive adhesive films, thermally conductive films in thermoelectric cooling devices, passivation films for integrated circuit devices (ICs), and field emission cathodes) |

Figure 5: Diamondoid-DNA cube-shaped nanostructured assembly: (i) Green dotted lines showing hydrogen bonding between complementary sequences. (ii) Electrostatic potential surface of the cube-shaped nanostructure, where the red regions bear negative partial charges whereas the positive sites are colored in blue. (iii) The Corey-Pauling-Koltun model of the same nanostructure reflecting the square shape of each face.

Table 1: Major Applications of Diamondoids and Derivatives.
diamondoids derivatives are an important family of compounds able to render diverse, strong, and sometimes unique biological properties to a multitude of drug classes. As many of these molecules are still in initial development phases, it will not be surprising if a considerable amount of new cage compounds start to be a good addition to our medical supplies in a near future [6].

In Table 1 we report an alphabetical list of applications of diamondoids in biomedicine, materials science, nanotechnology. Diamondoids are fascinating molecules with interesting and promising applications as molecular lego in biomedicine, materials science, and nanotechnology. Recently a book (Figure 6) was published in which the details of diamondoids sources, properties and applications were reported.

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