Magnetosomes: The Bionanomagnets and Its Potential Use in Biomedical Applications

Abstract

Magnetotactic Bacteria (MTB), a Gram negative, polyphyletic group of the domain Bacteria has gathered all the attention for its unique synthesis of bionanomagnets, 'the magnetosomes'. Though discovered by Blakemore over forty years, it has still been a challenge to isolate and culture MTB due to its vast morphological, metabolic and phylogenetic diversity. The potential applications of magnetosomes are innumerable, the most focused being in the biomedical field. Advanced research is carried out in the treatment of cancer using animal models and scientists are now looking at MTB as the promising biosolution. The only limitation to its commercial use is the availability of magnetosomes. Till date, only a few MTB strains have been isolated and cultivated axenically. However, the magnetosome yield obtained from these strains is not sufficient for commercialization. Isolation of new wild type MTB strains with endogenously higher magnetosome yield is desirable. Therefore, it is required to explore diverse econiches in search of MTB, study their versatile metabolism and biomineralization process. Biosynthesis of large quantities of magnetosomes is currently the need for biomedical applications. The aim of this review is to highlight the immense potential of these bionanomagnets in the field of cancer treatment.

Keywords: Magnetosomes; Iron nanoparticles; Magnetic field; Biomedical applications; Cancer; Magnetic hyperthermia

Opinion

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Abbreviations: MTB: Magnetotactic Bacteria; SPION: Super Paramagnetic Iron Oxide Nanoparticles; MRI: Magnetic Resonance Imaging

Introduction

Magnetotactic bacteria (MTB) are a diverse group of bacteria that was discovered in 1975 by Richard Blakemore [1]. The striking feature of MTB is the synthesis of intracellular iron nanoparticles in biomembrane enveloped vesicles called magnetosomes. It is these magnetosomes that allow the bacteria to respond to an external magnetic field [1,2]. The advantage of using MTB is the fact that they produce nanosized (30-120 nm), membrane bound uniform crystals of magnetite or greigite intracellularly under ambient conditions and are single domained. These multi featured nanoparticles therefore attract attention for diverse biomedical and other technological applications. Another merit in using these bionanoparticles is the fact that the bacteria usually produce a chain of magnetosomes which function as a biological compass and allow the bacterium to migrate through the applied magnetic field [3-9]. These magnetic crystals enveloped in a biomembrane are an ideal platform for tagging a number of drugs, antibodies and other substances which can be channelized to the affected area through the application of external magnetic field [10-13]. This property has been explored by researchers in developing and designing different strategies in combating cancer [14-17].

Properties of magnetosomes:

The synthesis of magnetosomes by MTB is highly controlled and a systematic process. The uniformity and regularity of the crystal size is remarkable and suitable for biomedical applications. This uniformity in size and shape cannot be achieved in case of chemically synthesized iron nanoparticles. Secondly, the biomembrane surrounding the crystal is a bilayered membrane composed of lipids and small amounts of proteins thereby giving an overall negative charge [3,7,9,15]. Owing to these chemical groups, the magnetosome surface is easily vulnerable to functionalization as compared to its chemical counterpart [18]. The chain arrangement of magnetosomes is stable even after cell disruption. This is an important characteristic desired for biomedical application since it prevents aggregation and aids in the internalization of the chain within the human cells [15,16] especially the tumor cells [19]. It has been observed that live MTB administered intravenously have an inherent tendency to get attracted to the anoxic environment at the tumor site [19]. This feature of MTB can be attributed to the fact that MTB are naturally found in microaerobic habitats where there is low oxygen concentration since oxygen has an inhibiting effect on them [6]. This very property is crucial for biomedical applications.

Other properties of magnetosomes which make them superior to chemically synthesized iron nanoparticles include narrow size distribution, good dispersion in water, higher heating capacities and magnetism, thermally stable magnetic moment, higher degree of purity and crystallinity, stability at ambient temperature and ferrimagnetic in nature [3,4,15,20-22]. Bacterial magnetosomes are highly biocompatible and relatively less toxic to the cells [23-25]. It has been observed that while the dosage required for causing acute toxicity on administration of super paramagnetic iron oxide nanoparticles (SPION) in a rat model is 135 mg/

kg, toxicity with bacterial magnetosomes was noted at a much higher concentration of 480 mg/kg [23]. Bacterial magnetosome biodistribution studies reveal that when administered intravenously in mice [23] and rats [26], the magnetosomes are degraded intracellularly by the reticuloendothelial system from the blood stream and released as free iron. However, Alphandery et al. [15] have reported elimination of magnetosomes in the feces of rats following intratumoral administration. The bacterial magnetosomes unlike chemically synthesized iron nanoparticles can also be manipulated at the genomic and proteomic level [22,27].

Applications of magnetosomes and MTB:

Among the several biomedical applications, one of the most focused areas of research is the use of magnetosomes in the treatment of cancer using magnetic hyperthermia. It involves injecting the magnetic nanoparticles at the tumor site followed by application of an alternating magnetic field. This leads to generation of heat which causes anti-tumor activity. Since magnetosomes possess good heating property and respond to applied magnetic field, they are ideal candidates for the application in magnetic hyperthermia [16,17,23,28]. Magnetic Resonance imaging (MRI) is another important application wherein the magnetosomes have been used as contrast agents [29]. It has been reported that small sized magnetosomes produced a positive contrast which enhanced the visibility of MTB inside the tumor when injected intravenously. MTB group of bacteria particularly has great biomedical importance owing to the fact that they swim in the blood and have inherent tendency to target tumor sites as visualized using MRI [19]. Drug Delivery using magnetosomes is one of the best approach as the magnetosome membrane surface is covered with a number of chemical groups. These groups can be conjugated with antibodies or drugs and injected at the tumor sites. Using this approach, Sun et al. [12,13] have studied the effect of doxorubicin against hepatic cancer. According to this study, the anti-tumor activity increased and the mortality rate decreased using the magnetosome conjugated drug delivery. It was also observed that the drug is highly toxic with a mortality rate of 80% when injected solely however, when conjugated with magnetosomes the mortality rate decreased to 20%.

Other applications of magnetosomes include use in immunoassays, carriers of enzymes, drugs, antibodies [10-13], cell separation, detection of nucleotide polymorphism, DNA extraction [30], magnetic separation of heavy metals and radionuclides [31,32] etc. Live MTB can also be used in nanorobotics [33]. MTB can be propelled to any desired position by applying sufficient torque to the intracellular magnetosome chain under the influence of magnetic field.

Limitations in the use of magnetosomes for commercialization

Even though magnetosome research has shown promising advances, the only limitation in its commercialization is the availability of magnetosomes. As of now only upto 170 milligram of bacterial magnetosomes is being produced from one liter of the culture media per day using MTB strain, *Magnetospirillum gryphiswaldense* MSR-1 [22,34]. Large scale cultivation of MTB is desirable to obtain consistent magnetosome yields in order to commercialize them especially for biomedical applications.

Conclusion

Nanotechnology is evolving rapidly with a constant search for development of new therapies, processes and strategies to overcome the challenges and difficulties faced in any field of science. MTB has opened up new dimensions in the field of medicine and technology. However, the only limitation towards their potential applications includes isolation and cultivation of MTB axenically. It is extremely difficult to mimic the complex environment of the chemically stratified natural econiches under the artificial laboratory conditions. Therefore, till date only a few MTB strains have been purified and are being studied at the genome level for a better understanding of magnetosome synthesis and biomineralization process. MTB has become a subject of interdisciplinary research and there is a growing need to explore the diverse ecosystems in search of this polyphyletic group of bacteria. Therefore, this paper is mainly aimed at recognizing the biotechnological potential of these amazing live nanomagnets.

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