

The possible use of Nanotechnology in the treatment of Osteoporosis

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Abstract

The use of nanotechnology is ever developing within the medical field. Osteoporosis is becoming a more prevalent bone degeneration disease within society. Hence, biomaterials could be developed that create scaffolding matrices around deteriorating areas to produce layers of scaffolding to artificially synthesise bone cells composing of Hydroxyapatite, collagen, carbon nanotubes and calcium. The nanostructures would chemically interact with each other to disperse around the site with metallic bonding maintain the structural shape. The nanocomposite can interact with the bone structure at a nano level which treatments for osteoporosis currently do not involve thus remain fairly ineffective.

Osteoporosis is a degenerative bone condition wherein the strong honeycomb mesh of the trabecular bone struts become thin resulting in fragility thus are more prone to break after minor bumps. Fractures within the wrist, hips and spine are most frequent amongst sufferers. Figure 1 shows a section of osteoporotic bone in comparison to a normal one. Approximately 75 million people in Europe, US and Japan are affected (international osteoporosis foundation) reflecting the magnitude of prevalence.

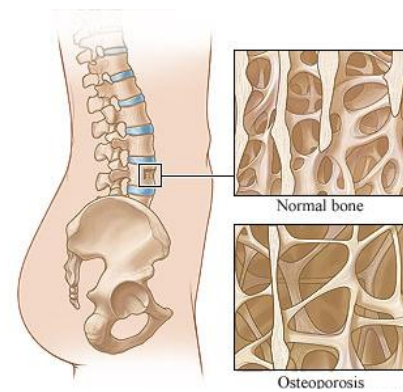


Figure 1

After the age of 35, bone loss increases very gradually as part of the natural ageing process. This bone loss becomes more rapid in women for several years following the menopause). This is due to oestrogen levels falling which results in quicker bone degradation than production consequently 1 in 3 women over 50 will experience osteoporotic fractures (international). The break that results can cause pain, disability and loss of independence, or even prove fatal, especially when it leaves an older person immobilised. Only one in three people return to their level of function after breaking a hip and one in five will require long term nursing care. This can be strain on medical resources in the time of recession.

Currently treatments for osteoporosis revolve around conservative, medical, surgical and alternative therapies. Supplement of Calcium and Vitamin D are given however studies show little effect (Jackson RD 2006). Hormone replacement therapy can be given to women suffering the condition but can increase the risk of other conditions including strokes and breast cancer. Surgery includes vertebroplasty which relieves pain from spinal compression fractures by injecting bone cement into joints though it does not provide a full long-term recovery method so is not effective for younger sufferers. On a whole most therapies only aim to maintain bone density instead of returning it to its former state. Consequently, new technology at the nanoscale needs to be developed which coincides with nature providing effective generation of bone tissue enabling

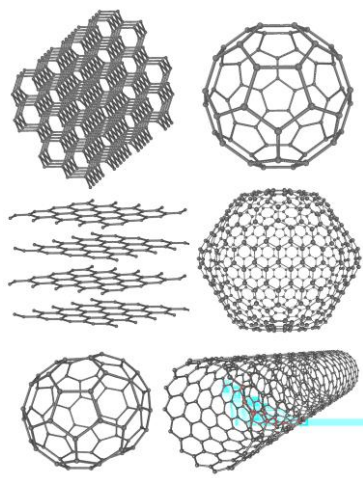


Figure 2

the treatment of osteoporosis.

Nanotechnology is the creation of useful materials, devices, and systems through the manipulation of matter on a minuscule scale: billionth of a meter. It is essentially mimicking

nature by 'building structures from atoms, not reducing something big to small'. Current advances in the region have been evoked by carbon nanotubes. These are hollow cylinders that form a hexagonal mesh with carbon atoms at each vertex. Figure 2 displays the structure of a carbon nanotube. These miniscule structures exhibit tremendous properties as they are stronger than steel in comparison to their density making them a suitable device for osteoporotic scaffolding implants. Nanotechnology is being applied to almost every field imaginable, including electronics, magnetics, optics, information technology, material development, and biomedicine. Due to their small size, nanoscale devices can readily interact with biomolecules on both the surface of and inside cells. By gaining access to so many areas of the body, they have the potential to detect disease and deliver treatment in ways unimagined before now (National Cancer Institute). The use of nanoparticles for the delivery of chemotherapy drugs directly to the tumour cells highlights the magnitude of recent technology. It enables drugs to be administered directly to the site of infection improving the effectiveness of treatment. Figure 2 also shows the structure of a 'Bucky ball' (Buckminsterfullerene) which was founded by Dr. Richard E. Smalley in 1985 that consists of 60 carbon atoms bonded together with a hollow centre ideal for drug administration (nanotechnology now) which provides the capsule for drug delivery. Moreover, nanobotic treatments have evolved such as vascular surgery; by nanorobots being introduced into the vascular system also, bio implantable sensors that bridge the gap between electronic and neurological circulatory.

Although advances in several critical research field have started to benefit from nanotechnology, to date, relatively few advantages have been described for biological application specially those involving the treatment of bone disorders. (Peppas et al 2007). This is despite the fact that bone itself is a nano-structured material composed of biological entities like proteins and hydroxyapatite crystals that have nanometer dimensions (Rho *et al* 1998). As a result a new treatment for osteoporosis needs to be evolved that lies on the basis of repairing and regenerating the damaged bone cells whilst maintaining its mechanical properties with the patient incurring the least possible form of discomfort. During this paper this notion will be addressed to see if nanotechnology can enable a hexagonal scaffolding structure to be created that attaches to the site of deterioration to induce bone cell regeneration resulting in permanent strengthening after which it degenerates itself.

Discussion

An ideal therapeutic nanomaterial is hoping to be developed that aids regeneration and strengthening of the bone that restricts its activity only to the site of degradation within the trabecular bone struts with miniscule effects on the surrounding tissue it. A carbon based nanostructure that ultimately provides scaffolding specifically directed at osteoblasts in the affected area for the promotion of new bone cells will be investigated to see if it could be used to encapsulate the deteriorating bone and prohibit further osteoporosis.

The extra cellular matrix of the bone has two main components: the organic collagen fibrils and the inorganic bone crystals referred to as hydroxyapatite. Collagen is one of the most abundant proteins in the body. Professor Buehler, Principal Investigator at the Atomistic Mechanics Modeling Laboratory at MIT investigated a breakthrough in understanding how molecular and tissue properties are linked. The smallest building blocks of collagen, called tropocollagen molecules, are five to ten times stronger than steel, while sustaining enormous tensile strains of up to fifty percent before fracturing. Nature takes advantage of the nanoscale properties of individual molecules at larger scales, leading to a tough material. This is

achieved by arranging tropocollagen molecules into a staggered assembly known as collagen fibrils. “The natural design represents a delicate balance between tensile forces within each tropocollagen molecule and shear forces between the molecules,” says Buehler ([www.mit](http://www.mit.edu)). Collagen forms porous fibrils that enable bone mineralisation by providing the aqueous compartment in which mineral grows. Therefore, the nano material that needs to be developed must mimic the structure of collagen as it aids bone regeneration.

Hydroxyapatite is a hydrated calcium phosphate ceramic which has a structure similar to bones found in mammals and is classed as bioactive. This means it supports in growth by integrating into the surrounding bone structure without dissolving. The collagen provides a matrix for the phosphate to crystalline and increase density. Consequently, the artificially induced nano structure must also perform a similar role.

Furthermore, the administration of the nanomaterials needs to be explored. Administration needs to be effective so that bone growth is particularly stimulated at the site of deterioration and not in other areas. Consequences could lead to bone deformities resulting from cancerous bone growth in unrequired regions of bone or inducing growth of the incorrect type of cells. For the treatment of osteoporosis it is the osteoblasts that need to be initiated. A reduction in the flexibility of the joints may also arise with the incorrect administration which could lead to further disabling problems for patients. Magnetic coated nanoparticles could be utilised by being directed to the site using an external magnetic field. This would ensure safe deploy of the nano scaffolding particles. Recently, hydroxyapatite coated magnetic nanoparticles synthesis was accomplished when studying osteoblasts cell activity. (G. Balasundaram, unpublished). They could be directed to the scaffolding onto which the rest of the nano materials would be covalently bonded to. Then their biomedical application would involve an inhomogeneous external magnetic field exerting a force upon them so they can be directed by a magnetic field gradient.

The strength of the nanostructure scaffolding which is to be evolved depends on the arrangement of carbon atoms. Diamond, the strongest natural mineral, has a crystalline structure of carbons. This ensures strong covalent bonding throughout the structure at a balanced level. However diamond is a macro-molecular structure; the converse of such a structure is required in this context. Strength needs to be administered via a small structure so that it can encapsulate the affected area. Another regular carbon pattern is found in graphite. Graphite contains small layers of carbon atoms arranged in a hexagonal shape with strong covalent bonding acting throughout the entire layer. Moreover, metallic bonding takes place between these layers between the delocalised valence electrons and ions. Using this information, we are at reasonable knowledge to purpose a structure for the carbons, which is small as well as strong. It requires carbon that is bonded in a singular hexagonal shape. Each carbon has two bonds, leaving the other two free. Therefore the carbon can form an ion with a 2+ charge. Leaving the 2 free electrons to form a sea around the molecule, this will be used to form metallic bonding to support the whole structure around the bone. Also could these electrons be used to ensure the carbon hexagon attaches to the bone securely? The scaffolding idea can be formed using multiple hexagons, in a crystalline formation. This would then create two layers of carbon, which are complementary to each other. However, how can this structure be achieved along the bone, whilst ensuring the structure is kept in its required formation? The formation of these hexagons would also require controlling. We could use a common technique used in the manufacture of plastics. Plastics are polymers, eg polyethylene. To ensure the plastic forms in the required manner a certain catalyst is used. A different catalyst is used for a different percentage of bonding. Therefore something similar could also

be done within the bone. A catalyst could be used to ensure the hexagons form in the desired pattern, we don't know yet, due to lack of research in this field, but the catalyst could be as simple as water. The most important aspect of the catalyst is that only small amounts will be needed. This is due to the nature of the catalyst being reused, as by the end of a 'reaction' the catalyst does not change chemically. The bioceramic nanomolecules that form react in a hydrolysis reaction to form single monomers thus stopping further growth of scaffolding. The scaffolding created would be porous in structure with aqueous compartments in which the bone cells replicate.

At present artificial bone scaffolding created from single walled carbon nanotubes have developed. The strength, flexibility and light weight of SWNT's enable them to act as scaffolds by mimicking the composition of collagen and inducing the growth of hydroxyapatite crystals. Bone cells can grow and proliferate on a scaffold of CNTs as they are not biodegradable and behave like a matrix onto which new cells can implant and form living tissue which becomes normal functioning bone. (nanoBio Technology).

Current tendency in bone tissue engineering is developing materials that temporarily substitute for the bone while inducing its regeneration in such a way that this, temporary material, disappears as the bone recovers its space. Ms Beatriz Olalde, researcher at the Health Unit of Tecnalia, is working on the creation of one of these compounds. With the results obtained to date, she has presented her PhD thesis at the University of Basque Country (UPV/EHU), entitled, *Development of a new porous, biodegradable nanocompound support for the regeneration of bone tissue*.

The porous support or foam, developed by Ms Olalde and defended in her thesis, is totally new. The aim was to manufacture a biodegradable porous support which, while temporarily substituting for the damaged bone, would be capable of inducing a process of bone regeneration. With this in mind, a compound was developed which is capable of interacting chemically and electrically with the bone cells or the adjoining bone tissue, thus accelerating bone recovery. The basis of the composition of the porous support presented in the thesis is a polymer: polylactic acid, a material widely used in medicine and which, given its biodegradable properties, disappears as the bone grows. To this the researcher added a bioceramic — hydroxyapatite. Polymers have difficulties in attracting cells and so the function of hydroxyapatite, which provides calcium, is facilitating this integration of the support into the surrounding bone cells. Finally, the compound also has carbon nanotubes. These enhance the mechanical properties of the polymers, which are limited in this aspect and would otherwise break up given bone resistance. Moreover, it is the carbon nanotubes that provide the electrical character to the porous support, as both the polylactic acid and the hydroxyapatite are insulating materials. In this manner, an electric field can be applied in such a way that the bone cells are directed to the porous support and the regeneration process is accelerated. According to Ms Olalde in her thesis, the trials undertaken with the new porous support, involving both in vitro and in vivo experiments, gave satisfactory results. The foam proved to have optimum mechanical properties for supporting the bone well and, moreover, it does not break up once implanted. What is more, with the initial in vivo results, obtained 3 weeks after being implanted in the porous support, bone growth was already observed. Also, after 16 weeks, this new bone showed mechanical, histomorphometric and densitometric properties similar to those of intact or healthy bone tissue. (nanomagazine.co.uk)

Conclusion

Currently, orthopaedic implants are not efficient enough to mimic optimal bone material that can help effectively strengthen the degenerated bones in osteoporosis for a long term period. A bone regeneration material is required that imitate the natural scientific structure of the bone enabling effective bone reconstruction resulting in permanent and long-lasting treatment. Therefore it is proposed that a development could emerge involving the use of nanobiological substances. As a result structures which are similar to the nanofeatures of the bone could be developed which can imitate the natural structure of the bone enabling the degeneration in osteoporosis being overcome after treatment. Not only will these nanomaterials encapsulate the deteriorated site, but will also interact with the cell surface of the bone at a miniscule level resulting in adherence of the new tissue formation strengthening the bone structure. However we must stress that further research will need to delve into inexpensive fabrication techniques which are currently being investigated.

To conclude, this research has shown that nanotechnology can be used to cure osteoporosis. Using a material made using a polylactic acid, hydroxyapatite and carbon nanostructures. We have explained the structure of the carbons to create strong scaffolding, whilst the bone is healing. Also the material being degradable after it is no longer needed. We have also explored that the way to get the carbons to line up in a regular, tough way is to use a catalyst. Therefore a material made of polylactic acid, hydroxyapatite and a carbon hexagon structure can be used to cure osteoporosis. It can offer structural support, as well as physical. With the right research and funding this structure or something similar could be created and used in modern day medicine.

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Figure 1 www.webmd.com/osteoporosis/tc/osteoporosis-treatment-overview

Figure 2 www.chem.wisc.edu/~newtrad/CurrRef/BDGTopic/BDGtext/dmndref.html

Collagen structure deciphered

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jbc journal of biochemistry <http://www.jbc.org>

nano, the magazine for small science www.nanomagazine.co.uk