AMERICAN JOURNAL OF PHARMTECH RESEARCH
Journal home page: http://www.ajptr.com/

The Role of Buckminster Fullerenes in Preventing Allergy

Subashini Rajakannu[1*], Pooja Chandrasekaran[2], Banu saranya Arumugasamy[2]
1. Assistant Professor, Department of Biomedical Engineering, SSN College of Engineering, Kalavakkam, Chennai – 603 110, Tamil Nadu, India.
2. Department of Biomedical Engineering, SSN College of Engineering, Kalavakkam, Chennai – 603 110, Tamil Nadu, India.

ABSTRACT

Nanotechnology plays a major role in the medical field for treating various pathological conditions, but the field of nanoimmunology has not developed to full extent. This paper presents about the role of nanoparticle in treatment of allergy. Mast cells and peripheral blood basophils are the cells mainly responsible for allergy. When a foreign particle enters the body, the immune system is activated and they produce certain molecules (mostly immunoglobulins, IgE). Histamines are also produced by the mast cells which affect the local areas, thus, stimulating the production of immunoglobulins. This review explains how allergies can be cured by using buckminster fullerenes (buckyballs). The fullerene attaches with mast cells and basophils, and then inhibits activation of IgE receptor. However, the major disadvantage of using buckyballs is its toxicity. Fullerene molecules in water form oxygen free radicals which in turn react with the lipid molecules present in the cell membrane. The lipid molecules form free radicals which lead to rupture of cell membrane on interacting with water present outside the cell. But the toxicity can be reduced by surface modifications. Therefore the surface of buckyballs can be modified on reaction with 24 OH groups and 3 COOH groups to reduce toxicity. The COOH and OH side groups make the buckyball derivatives more water soluble. Therefore they are less likely to form clumps. The advantages of using fullerenes is that it does not have side effects that certain anti-allergic drugs have and is highly effective in reducing allergic responses.

Keywords: Allergy, Mast Cells, histamine, Buckminster Fullerene, Immunoglobulins.

*Corresponding Author Email: subashinir@ssn.edu.in
Received 12 November 2014, Accepted 17 November2014

Please cite this article as: Subashini R *et al.*, The Role of Buckminster Fullerenes in Preventing Allergy. American Journal of PharmTech Research 2014.

INTRODUCTION

An allergy is a hypersensitivity disorder of the immune system. Allergic reactions occur when a person's immune system reacts to normally harmless substances in the environment. A substance that causes allergic reaction is called an allergen. These reactions are acquired, predictable, and rapid. Allergic reactions are distinctive because of excessive activation of certain white blood cells called mast cells and basophils by a type of antibody called immunoglobulin E (IgE). This reaction results in an inflammatory response. While most of the allergic responses cause discomfort, sometimes it may be fatal (such as anaphylactic shock) [1]. IgE is produced by plasma cells located in lymph nodes draining the site of antigen entry or locally, at the sites of allergic reactions, by plasma cells derived from germinal centers developing within the inflamed tissue. IgE is located predominantly in tissues, where it is tightly bound to the mast-cell surface through the high-affinity IgE receptor. Binding of antigen to IgE cross-links these receptors and this causes the release of chemical mediators from the mast cells such as histamine, heparin and a number of cytokines, which are rapidly released into the tissues and blood, leading to the development of a hypersensitivity reaction[2].

Action of Histamine

After the release of histamine by the mast cells, it binds with histaminergic receptors (H_1, H_2, and H_3) to elicit a series of events that mediates the characteristic responses through second messenger systems. The histaminergic receptors are G-protein coupled type. H_1 receptors are coupled to phospholipase-C and their activation leads to the formation of inositol phosphate (Ip_3) and diacylglycerol (DAG), respectively, from phospholipids in cell membrane. Ip_3 causes rapid release of Ca^{2+} from endoplasmic reticulum. The release of histamine, in addition to the stimulation of IgE receptors, also activates the phospholipase A_2, leading to the production of host mediators, including platelet activating factors and metabolites of arachidonic acid. Leukotriene D_4 is also generated, which is a potent constrictor of smooth muscles. This mediates the constriction of bronchi, leading to cough (in case of nasal allergy). Systemically, histamine contracts smooth muscles of the lungs and the gastrointestinal system and cause vasodilation, low blood pressure, and increases the heart rate [3]. It also causes symptoms such as itching, sneezing, watery eye, and running nose [4]. The objective of the paper is to provide an overview on the applications of Buckminster Fullerenes for the prevention of allergy.

Conventional treatments and their disadvantage

Allergy treatments involve usage of antihistamines, which block the histamine from working (E.g.

loratidine) and decongestants, in case of nasal problems. In some cases, immunotherapy is involved, in which allergens are injected. However, usage of antihistamines may lead to side effects such as drowsiness, dry mouth, cardiac arrhythmia and increase in blood pressure in case of decongestants[5]. Immunotherapy entails the risk of systemic anaphylactic reactions. Hence this review focuses on application of Fullerenes in clinical diagnostic tools for the treatment of allergy caused due to various factors.

Buckminster Fullerene

Buckminster fullerenes (C_{60}) are allotropes of carbon which are hollow balls (in the shape of a soccer ball) with 20 hexagons and 12 pentagons, where no pentagons share a vertex) with a carbon atom at the vertices of each polygon and a bond along each polygon edge. The Van der Waals diameter of a C_{60} molecule is about 1.01 nanometers (nm). The nucleus to nucleus diameter of a C_{60} molecule is about 0.71 nm. The C_{60} molecule has two bond lengths. The 6:6 ring bonds (between two hexagons) can be considered "double bonds" and are shorter than the 6:5 bonds (between a hexagon and a pentagon). Its average bond length is 0.14 nm. Each carbon atom in the structure is bonded covalently with 3 others [6].

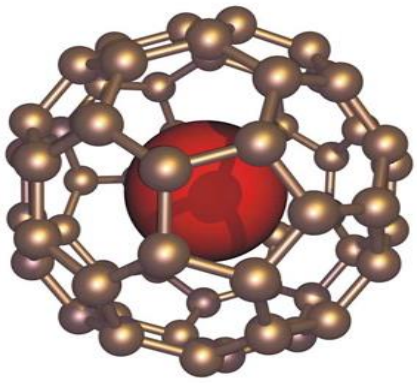


Figure.1.Graphical Representation of a Fullerene

Physical properties of buckminster fullerenes

The fullerenes (C_{60} and other relatives) are remarkable molecules in that they are exceedingly rugged, very stable, and capable of surviving the temperatures of extreme outer space. They can survive collisions with metals and other materials at speeds in excess of 32,000 kilometres per hour, a speed that would tear most organic molecules apart they react with elements from across the periodic table and with the chemical species known as free radicals. They have rugged structure and high reactivity. They can survive collisions with metals and other materials at speeds in excess of 32,000 kilometres per hour, a speed that would tear most organic molecules apart. These

superconducting buckyballs have the highest critical temperature of any known organic compound, withstanding temperatures up to 18K[7].

Action of buckyballs

Human mast cells (MC) and peripheral blood basophils are critical cells involved in the initiation and propagation of several inflammatory conditions, mainly type I hypersensitivity. Fullerenes are a negative regulator of allergic mediator release that suppresses Ag-driven type I hypersensitivity. Spleen Tyrosinase Kinase, also known as SYK, is an enzyme which regulates the transmission of signals from B-cells and T-cells. It transmits the signals generated by immune reactions to mast cells and basophils, which in turn, release histamines. Buckyballs inhibit the phosphorylation of SYK [8, 9]. This, in turn, impedes the transmission of signals. In addition, fullerene preincubation significantly inhibits IgE-induced elevation in cytoplasmic reactive oxygen species levels[10]. Furthermore, fullerenes prevent the in vivo release of histamine and drop in core body temperature[11]. As it is inert, it does not react much with the body fluids shown in figure 2.[8]

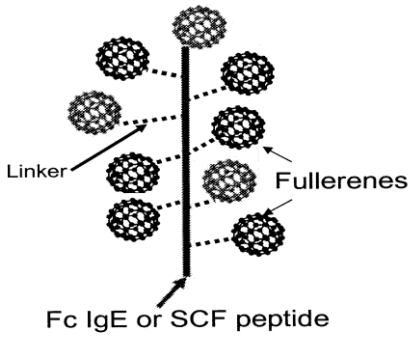


Figure 2. Action of Bucky balls on IgE

Disadvantages of buckyballs

Fullerene molecules in water form oxygen free radicals which in turn react with the lipid molecules present in the cell membrane. The lipid molecules form free radicals which lead to rupture of cell membrane on interacting with the water present outside the cell [12]. Buckyballs dissolved in water, group together into clumps known as nano-C60, which is more toxic to the human skin cells (more than half of the skin cells can die at the concentration of 20 ppb. On prolonged exposure, it accumulates in the human body. It also travels through the mother's placenta.

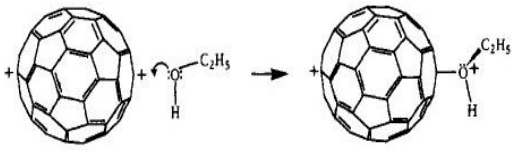
Toxicity Reduction

It has been found that level of toxicity of bucky balls is inversely related to the degree of surface modification. Cytotoxicity can be greatly reduced by chemically modifying the buckyballs' surface.

Differences in cytotoxicity seem to be due to the relative solubility of the nanoparticles. It is known that pristine buckyballs are partially soluble in water, forming clumps. The side groups make the buckyball derivatives more water soluble and less likely to form clumps. Buckyballs with three COOH side groups had a LC_{50} value of 10,000 ppb, while for those with 24 hydroxyl side groups it was over 5m ppb. Usually, -OH groups and –COOH groups are preferred [13, 14, 15]. Some examples of OH groups that can be added are: H_2O, CH_3OH, C_2H_5OH and n-C_3H_7OH.

The various mechanisms by which fullerenes react with OH groups are:

1. Nucleophilic addition:



2.Hydroxide abstraction channel

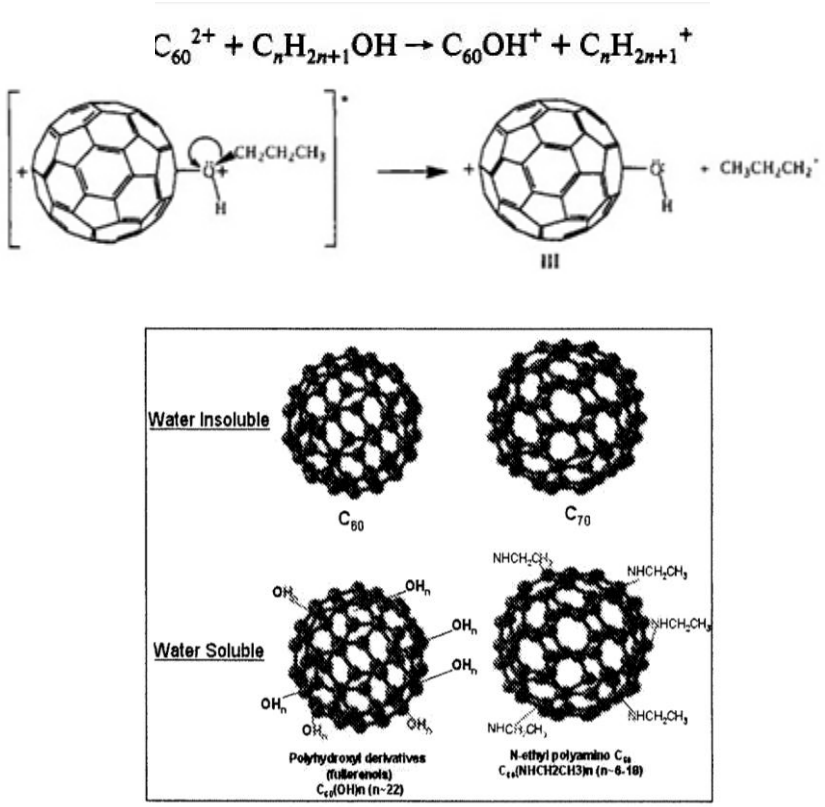


Figure 3. Fullerenes before and after surface modification[8]

The more the fullerene surface is modified, the lesser becomes its toxicity. Thus, the surface of fullerenes should be modified to the possible extent to reduce the toxicity[15].

CONCLUSION

Fullerenes, which have been used in medicine primarily for diagnostic purposes, can be exploited in anti-allergy treatment. The main advantage over conventional treatment is that anaphylaxis is reduced in this method. The toxicity is reduced if derivatives of fullerenes are used. Apart from type I hypersensitivity, type IV can also be treated by this method (allergies due to rejection of organ implants).The application can also be extended to Killing of tumour cells by releasing free radicals and in novel drug-delivery systems.

REFERENCES

1. Simons F, Estelle R. Anaphylaxis. Journal of Allergy and Clinical Immunology. 2010; 125(2): S161 - S181.
2. Janeway CA Jr, Travers P, Walport M, et al. Immunobiology: The Immune System in Health and Disease. 5th edition. New York: Garland Science; 2001.
3. Dean Befus A, Mowat C, Gilchrist M, Hu J, Solomon S, Bateman. A. Neutrophil Defensins Induce Histamine Secretion from Mast Cells: Mechanisms of Action. The Journal of Immunology. 1999; 163: 947-953.
4. Akdis, CA, Blaser K. Histamine in the immune regulation of allergic inflammation. Journal of Allergy and Clinical Immunology. 2003; 112: 15 – 22.
5. Dora L, Ahmet A, Ward L, Krishnamoorthy P, Efrem DM, Richard L, Jacques PB, Albert C, Harold K. A practical guide to the monitoring and management of the complications of systemic corticosteroid therapy. Allergy, Asthma & Clinical Immunology. 2013: 9:30.
6. Goyal A, Trivedi NK, Arora A. Bucky ball: as novel nanomaterial. International Journal for Phramaceutical Research and Development.2009; 8:1-12.
7. KK Jain - The Handbook of Nanomedicine, 2008 – Springer.
8. Ryan JJ, Bateman HR, Stover A, Gomez G, Norton SK, Zhao W, Schwartz LB, Lenk R, Kepley CL. Fullerene Nanomaterials Inhibit the Allergic Response. Journal of Immunology. 2011; 179: 665-672.
9. Kepley CL. Antigen-induced reduction in mast cell and basophil functional responses due to reduced Syk protein levels. Int. Arch. Allergy Immunol. 2005; 138: 29-39.
10. Siraganian RP, Zhang J, Suzuki K, Sada K. Protein tyrosine kinase Syk in mast cell signaling. Mol. Immunol. 2002; 38: 1229-1233.
11. Takano T, Sada K, Yamamura H. Role of protein-tyrosine kinase syk in oxidative stress signaling in B cells. Antioxid. Redox Signal. 2002; 4: 533-541.

12. Dellinger A, Brooks DB, Plunkett B, Vonakis BM, Sandros M, Zhou Z, Kepley CL. Effects of Novel Nanomaterials on Allergic Mediator Release from Human Mast Cells and Basophils through Non-IgE Mediated Pathways. J Nanomed Nanotechol. 2013; 3:1-8.
13. Wani MY, Hashim MA, Nabi F, Malik MA. Nanotoxicity: Dimensional and Morphological Concerns. Advances in Physical Chemistry. 2011; 15 p
14. Johnston HJ, Hutchison GR, Christensen FM, Aschberger K, Stone V. The Biological Mechanisms and Physicochemical Characteristics Responsible for Driving Fullerene. Toxicity Toxicol. Sci. 2010; 114 (2): 162-182.
15. Javahery G, Petrie S, Wmcel H, Wang J, Bohme DK. Gas Phase Reactions of the Buckminsterfullerene Cations C60*+, C6O2+, and C60g3+ with Water, Alcohols, and Ethers . J. Am. Chem. SOC. 1993; 115: 6295-6301.