



Nanoburrs: A Novel Emerging Drug Delivery System to Tackle Cardiovascular Disease - A Review

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ABSTRACT

The advents of nanotechnology lead to invention of many dosage forms. Targeting drug delivery has long been a problem for medical researchers i.e., how to get them to the right place in the body and how to control the release of the drug to prevent overdoses. The development of new and complex molecule called Nanoburrs has the potential to solve this problem. Targeted nanoparticles that can cling to artery walls and slowly release medicine, an advance that potentially provides an alternative to drug-releasing stents in some patients with cardiovascular disease. The particles, dubbed "nanoburrs" because they are coated with tiny protein fragments that allow them to stick to target proteins, can be designed to release their drug load over several days. The nanoburrs are targeted to a specific structure, known as the basement membrane, which lines the arterial walls and is only exposed when those walls are damaged. Therefore, the nanoburrs could be used to deliver drugs to treat atherosclerosis and other inflammatory cardiovascular diseases." Patients with narrowed arteries in which drug-eluting stents cannot be used, now can use nanoburrs. Nanoburrs provides an advance technology in the field of science that potentially provides an alternative to drug-releasing stents in some patients with cardiovascular disease. Nanoburrs can also be used in other important diseases like cancer and inflammatory diseases where vascular permeability or vascular damage is commonly observed. This review brings about the working and applications of nanoburrs.

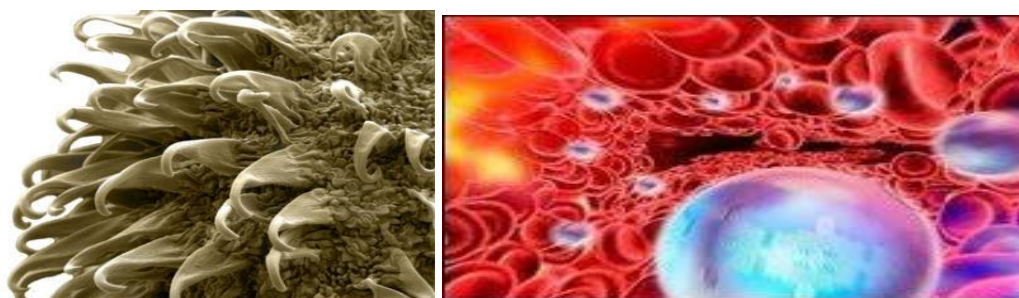
Keywords: Nanoburrs, Nanotechnology, Nanoparticles, cardiovascular disease.

INTRODUCTION

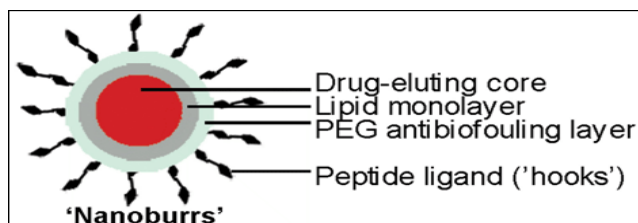
The drug delivery technology has certainly a new interest for drugs by providing them new life through their therapeutic targets. Nowadays, targeting drug delivery is the major problem which is being faced by the researchers. Target oriented drug administration with improvements in therapeutic efficacy, reduction in side effects and optimized dosing regimen, shall be the leading trends in the area of therapeutics. Targeted drug delivery implies for selective and effective localization of pharmacologically active moiety at preidentified (preselected) target in therapeutic concentration, while restricting its access to non-target normal cellular linings and thus minimizing toxic effects and maximizing therapeutic index of the drug. Targeted drug delivery is the delivery of drug to receptor, organ or any part of the body to which one wishes to deliver the drug exclusively. Effective targeted drug delivery systems have been a dream for long time, now but it has been largely frustrated

by the complex chemistry that is involved in the development of new systems. Targeting drug delivery has long been a problem for medical researchers i.e., how to get them to the right place in the body and how to control the release of the drug to prevent overdoses. The development of new and complex molecule called Nanoburrs has the potential to solve this problem.

Nanoburrs are tiny particles that travel through the bloodstream and attach to affected arteries where they deliver medicine directly to damaged tissue. Nanoburrs are coated with tiny protein fragments that allow them to stick to damaged arterial walls. Once stuck, they can release drugs (such as paclitaxel, which inhibits cell division and helps to prevent the growth of scar tissue that can clog arteries). The nanoburrs are targeted to a specific structure, known as the basement membrane, which lines the arterial walls and is only exposed when those walls are damaged.¹⁻²



'Nanoburrs' only stick to damaged areas of the artery



Therefore, the nanoburrs could be used to deliver drugs to treat atherosclerosis and other inflammatory cardiovascular diseases or in patients with narrowed arteries. Nanoburrs structure could make it easier to manufacture, because the targeted peptides are attached to an outer shell and not directly to the drug-carrying core, which would require a more complicated chemical reaction. This design also reduces the risk of the nanoparticles bursting and help in releasing the drugs safely.³

Medicated Stents v/s Nanoburrs

Essentially, nanoburrs are tiny particles that travel through the bloodstream and attach to affected arteries where they deliver medicine directly to damaged tissue. At first glance, they appear to work in a similar manner as medicated stents, the standard treatment for clogged arteries. A second look, however, shows that nanoburrs are a different type of answer to a far more complex question.

Currently, one of the standard ways to treat clogged and damaged arteries is by implanting a vascular stent, which holds the artery open and releases drugs such as paclitaxel. The researchers hope that this new nanoburrs could be used alongside such stents or in lieu of them to treat damage located in areas not well suited to stents, such as near a fork in the artery. Stents are very good at holding arteries open and preventing sudden collapse. They can also deliver life-saving medicine to damaged artery walls. However, a stent is stationary, posed like a tiny Atlas shouldering the weight of a sagging artery wall.⁴⁻⁵

Nanoburrs, on the other hand, can spread over scattered areas, yet target only damaged tissue. They stick like Velcro to target proteins that are found only with certain types of tissue damage

Preparation of Nanoburrs

A short peptide sequences of seven-amino-acid as called C-11 bind to molecules on the surface of the basement membrane. These were later used to coat the outer layer of the nano particles. The inner core of the 60-nanometer-diameter particles carries the drug, were bound to a polymer chain called Poly Lactic Acid (PLA). A middle layer of soybean lecithin, a fatty material, lies between the core and the outer shell, consisting of a polymer called Polyethylene Glycol (PEG) that protects the particles as they travel through the bloodstream. The drug can only be released when it detaches from the PLA polymer chain, which occurs gradually by a reaction called ester hydrolysis. The longer the polymer chain, the longer this process takes and thus the timing of the drug's release can be changed by altering the chain length of polymer.⁶ MIT and Harvard

researchers have designed new particles which they call nanoburrs can cling to damaged artery walls and slowly release cancer drugs with nanoparticles to clear cardiovascular disease.

Mechanism of Nanoburrs

The nanoburrs latch onto injured arterial walls because they're decorated with peptides pulled from bacterial phages, viruses that infect bacteria. It was found through research that one peptide latches onto the collagen that makes up the basement membrane of arteries which makes this peptide useful in preferentially binding to the basement membrane of the artery wall that gets exposed whenever the artery is injured, such as during an angioplasty, where the inflated angio balloon squeezes against the arterial wall, pulling off the top layer of cells. The nanoburr's stickiness means these tiny hybrid-polymeric particles are much more likely to hit the treatment target than nanoparticles lacking the protein hooks. In the current study, done in both arterial cell cultures in a dish and in the carotid arteries of living rats, the burred nanoparticles were between two and four times as likely to glom onto injured arterial tissue as non-burred varieties.⁷⁻⁸

Flexibility of Nanoburrs in Body

Process to keep the nanoburrs sticking and circulating in the blood for a long time is necessary for cardiovascular disease patient because as soon as it enters the patient body then body's natural defenses will quickly muster attacks against it, treating as a foreign particle for the body. To prevent this, nanoburrs are to be covered in soy lecithin, a fatty substance and then later should be coated with polyethylene glycol (PEG) because PEG is an inert hydrophilic substance and is able to evade much of the body's defenses. The researchers claim that the nanoburr's structure could make it easier to manufacture, because the targeted peptides are attached to an outer shell and not directly to the drug-carrying core, which would require a more complicated chemical reaction. The design also reduces the risk of the nanoparticles bursting and releasing drugs prematurely. They can be injected intravenously at a site distant from the damaged tissue. Because the particles can deliver drugs over a longer period of time, and can be injected intravenously, patients would not have to endure repeated and surgically invasive injections directly into the area that requires treatment.

Advantages of Nanoburrs

1. They can attach to damaged arterial walls and can release drugs (such as paclitaxel) to treat damage areas.
2. They can be injected intravenously at a site distant from the damaged tissue. Through research in rats; it was found that nanoburrs injected near the tail were able to reach the intended target i.e. the walls of injured carotid artery at twice rate than the stents but not normal carotid artery.

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Uses of Nanoburrs

1. Nanoburrs can be used in various cardiovascular diseases.
2. The nanoburrs could be used to deliver drugs to treat atherosclerosis.
3. Nanoburrs can also be used in other important diseases like cancer and inflammatory diseases where vascular permeability or vascular damage is commonly observed.

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