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A REVIEW ON LYMPHATIC CIRCULATION

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ABSTRACT

The circulatory system processes an average of 20 liters of blood per day through capillary filtration which removes plasma while leaving the blood cells. Roughly 17 liters of the filtered plasma actually get reabsorbed directly into the blood vessels, while the remaining 3 liters are left behind in the interstitial fluid. The primary function of the lymph system is to provide an accessory route for these excess 3 liters per day to get returned to the blood. The pressure in the venous system is considerably lower than the pressure in the arterial system. It contains a larger portion of blood than the arterial system does, for the venous system is thought to be the blood reservoir of the body. The lymphatic system can be thought of as a drainage system needed because; the blood circulates through the body, blood plasma leaks into tissues through the thin walls of the capillaries nanotechnology for treatment, diagnosis, monitoring, and control of biological systems. The use of Nanotechnology in medicine and more specifically drug delivery is set to spread rapidly.

INTRODUCTION

The lymphatic system is part of the circulatory system, comprising a network of conduits called lymphatic vessels that carry a clear fluid called lymph (from Latin *lympha* "water goddess") directionally towards the heart. The lymphatic system was first described in the seventeenth century independently by OlausRudbeck and Thomas Bartholin. The lymph system is not a closed system. The circulatory system processes an average of 20 litres of blood per day through capillary filtration which removes plasma while leaving the blood cells. Roughly 17 litres of the filtered plasma actually get reabsorbed directly into the blood vessels, while the remaining 3 litres are left behind in the interstitial fluid. The primary function of the lymph system is to provide an accessory route for these excess 3 litres per day to get returned to the blood. Lymph is essentially recycled blood plasma.

Lymphatic organs play an important part in the immune system, having a considerable overlap with the lymphoid system. Lymphoid tissue is found in many organs, particularly the lymph nodes, and in the lymphoid follicles associated with the digestive system such as the tonsils. Lymphoid tissues contain lymphocytes, but they also contain other types of cells for support. The system also includes all the structures dedicated to the circulation and production of lymphocytes (the primary cellular component of lymph), which includes the spleen, thymus, bone marrow, and the lymphoid tissue associated with the digestive system.

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Drug targeting in lymphatic circulation [2]

Colloidal particles in the nanometre size range (less than 1 μm in diameter) can be engineered to provide opportunities for the site-specific delivery of drugs after injection into the general circulation or lymphatic systems. Targets include the liver (both Kupffer cells and hepatocytes), endothelial cells, sites of inflammation and lymph nodes. The size and surface of the particle are crucial factors in targeting, and the attachment of cell-specific ligands can lead to increased selectivity. The applications of such particle engineering are discussed in relation to conventional drugs as well as the emerging area of gene therapy.

The main problems currently associated with systemic drug administration are: even biodistribution of

pharmaceuticals throughout the body; the lack of drug specific affinity toward a pathological site; the necessity of a large total dose of a drug to achieve high local concentration; non-specific toxicity and other adverse side-effects due to high drug doses. Drug targeting, i.e. predominant drug accumulation in the target zone independently on the method and route of drug administration, may resolve many of these problems. Currently, the principal schemes of drug targeting include *direct application of a drug* into the affected zone, *passive drug targeting* (spontaneous drug accumulation in the areas with leaky vasculature, or Enhanced Permeability and Retention-EPR-effect), *'physical' targeting* (based on abnormal pH value and/or temperature in the pathological zone), *magnetic targeting* (or targeting of a drug immobilized on paramagnetic materials under the action of an external magnetic field), and *targeting using a specific 'vector' molecules* (ligands having an increased affinity toward the area of interest). The last approach provides the widest opportunities. Such pharmaceutical carriers as soluble polymers, microcapsules, microparticles, cells, cell ghosts, liposomes, and micelles have been successfully used for targeted drug delivery in vivo. Though the direct conjugation of a drug molecule with a targeted moiety is also possible (immunotoxin), the use of micro reservoir type systems provides clear advantages, such as high loading capacity, possibility to control size and permeability of drug carrier systems and use relatively small number of vector molecules to deliver substantial quantities of a drug to the target. The practical use of the listed systems and approaches for the delivery of therapeutic and diagnostic agents will be considered.

Advantages of lymphatic circulation [3, 4]

1. An open circulatory system is a system in which the heart pumps blood into the hemocoel which is positioned in between the ectoderm and endoderm. The fluid described in the definition is called hemolymph, or blood.
2. Hemolymph flows into an interconnected system of sinuses so that the tissues receive nutrients, fluid and oxygen directly. In animals that have an open circulatory system, there is a high percentage of the body that is blood volume.
3. In a closed circulatory system, blood flows from arteries to capillaries and through veins, but the tissues surrounding the vessels are not directly bathed by blood. Some invertebrates and all vertebrates have closed circulatory systems. A closed circulatory system allows more of a complete separation of function than an open circulatory system does. The blood volume in these animals is considerably lower than that of animals with open circulatory systems. In animals with closed circulatory systems, the heart is the chambered organ that pushes the blood into the arterial system. The heart also sustains the high pressure necessary for the blood to reach all of the extremities of the body.
4. In the closed circulatory system of mammals, there are two subdivisions the systemic circulation and the pulmonary circulation. The pulmonary circulation involves circulation of deoxygenated blood from the heart to the lungs, so that it may be properly oxygenated. Systemic circulation takes care of sending blood to the rest of the body. Once the blood flows through the system of capillaries at the body's tissues, it returns through the venous system. The pressure in the venous system is considerably lower than the pressure in the arterial system. It contains a larger portion of blood than the arterial system does, for the venous system is thought to be the blood reservoir of the body.
5. There are a variety of advantages to having a closed circulatory system. Every cell of the body is, at maximum, only two or three cells' distance from a capillary. There is the ability for such animals to have incredible control over oxygen delivery to tissues. A unique characteristic to closed circulatory systems is that capability for a closed circulation to include the process of ultrafiltration in blood circulation. Since the lymphatic system is included as part of the circulatory system because of its circulation of excess fluid and large molecules, it decreases the pressure in tissues that extra fluid increases.
6. One of the most important advantages of the setup of the closed circulatory system is that the systemic and pulmonary branches of the system can maintain their respective pressures.

METHODS OF PREPARATION OF NANOTECHNOLOGY

Bottom-up Methods for Making Nanotechnology Products [7]

There are two general ways available to produce nanomaterials. The first way is to start with a bulk material and then break it into smaller pieces using mechanical, chemical or other form of energy (top-down). An opposite approach is to synthesis the material from atomic or molecular species via chemical reactions, allowing for the precursor particles to grow in size (bottom-up). Both approaches can be done in either gas, liquid, supercritical fluids, solid states, or in vacuum. Most of the manufacturers are interested in the ability to control: a) particle size b) particle shape c) size distribution d) particle composition e) degree of particle agglomeration.

The structure and magnetic properties of $MnFe_2O_4$ ferrites have been investigated using five different preparation methods, including the ceramic technique, flash combustion, co-precipitation, sol–gel and citrate methods. The characteristics of one sample prepared by different methods have been studied to select the better method, i.e. the one that is the simplest and does not require an elaborate instrumental set-up. The results

indicated that the citrate method gives the lowest value for the lattice parameter and particle size (14.1 nm), while the highest values are obtained with the ceramic method. The smallest nanosizes were obtained in the citrate and flash methods (14.1 and 40.7 nm, respectively).

Magnetism in Mn-doped ZnO nanoparticles prepared by a co-precipitation method [5]

We report the synthesis of nominal 2 and 5 at % Mn-doped Zn. Rietveld refinement of xray diffraction data revealed that Mn-doped ZnO crystallizes in the monophasic wurtzite structure and the unit cell volume increases with increasing Mn concentration. DC magnetization measurements showed ferromagnetic ordering above room temperature with Hc~150 Oe for nominal 2 at % Mn-doped ZnO nanoparticles annealed at 675 K. A distinct ferromagnetic resonance (FMR) signal was observed in the EPR spectra of the 2 at % Mn-doped ZnO nanoparticles annealed at 675 K. EPR measurements were used to estimate the number of spins participating in ferromagnetic ordering. Of the total Mn present in the 2 at.% MnZnO lattice, 25% of the Mn2+ ions were responsible for ferromagnetic ordering, whereas nearly 5% of the Mn2+ ions remained uncoupled elf-Assembled Monolayers of Thiolates on Metals as a Form of Nanotechnology (isolated spins). A well resolved EPR spectrum of 5% Mn-doped ZnO samples annealed at 875–1275 K (g = 2.007, A = 80 G, D = 210 G and E = 15 G) confirmed that Mn was substitutionally incorporated into the ZnO lattice as Mn2+. On increasing the temperature of annealing beyond 1075 K an impurity phase emerges in both the 2 and 5%Mn-doped ZnO samples, which has been identified as a variant of (Zn1−XMn (II)X)Mn(III)2O4 with Tc~15 K. Our results indicate that the observed room temperature ferromagnetism in Mn-doped ZnO can be attributed to the substitutional incorporation of Mn at Zn-sites rather than due to the formation of any metastable secondary phases.

Preparation and characterization of nanometric Mn ferrite via different methods [6]

The structure and magnetic properties of MnFe2O4 ferrites have been investigated using five different preparation methods, including the ceramic technique, flash combustion, co-precipitation, sol–gel and citrate methods. The characteristics of one sample prepared by different methods have been studied to select the better method, i.e. the one that is the simplest and does not require an elaborate instrumental set-up. The results indicated that the citrate method gives the lowest value for the lattice parameter and particle size (14.1 nm), while the highest values are obtained with the ceramic method. The smallest nanosizes were obtained in the citrate and flash methods (14.1 and 40.7 nm, respectively).

How to prepare Nano particles [7]

In nanotechnology, a particle is defined as a small object that behaves as a whole unit with respect to its transport and properties. Particles are further classified according to diameter. Coarse particles cover a range between 10,000 and 2,500 nanometers. Fine particles are sized between 2,500 and 100 nanometers. Ultrafine particles, or nanoparticles, are between 1 and 100 nanometers in size. The reason for this double name of the same object is that, during the 1970-80s, when the first thorough fundamental studies with "nanoparticles" were underway in the USA (by Granqvist and Buhrman) and Japan, (within an ERATO Project) they were called "ultrafine particles" (UFP). However, during the 1990s before the National Nanotechnology Initiative was launched in the USA, the new name, "nanoparticle," had become fashionable (see, for example the same senior author's paper 20 years later addressing the same issue, lognormal distribution of sizes). Nanoparticles may or may not exhibit size-related properties that differ significantly from those observed in fine particles or bulk materials. Although the size of most molecules would fit into the above outline, individual molecules are usually not referred to as nanoparticles.

Nanoclusters have at least one dimension between 1 and 10 nanometers and a narrow size distribution. Nanopowders are agglomerates of ultrafine particles, nanoparticles, or nanoclusters. Nanometer-sized single crystals, or single-domain ultrafine particles, are often referred to as nanocrystals.

Nanoparticle research is currently an area of intense scientific interest due to a wide variety of potential applications in biomedical, optical and electronic fields although, in general, nanoparticles are considered a discovery of modern science; they actually have a very long history. Nanoparticles were used by artisans as far back as the 9th century in Mesopotamia for generating a glittering effect on the surface of pots.

Even these days, pottery from the middle ages and renaissance often retains a distinct gold- or copper-colored metallic glitter. This luster is caused by a metallic film that was applied to the transparent surface of a glazing. The luster can still be visible if the film has resisted atmospheric oxidation and other weathering.

The luster originated within the film itself, which contained silver and copper nanoparticles dispersed homogeneously in the glassy matrix of the ceramic glaze. These nanoparticles were created by the artisans by adding copper and silver salts and oxides together with vinegar, ochre, and clay on the surface of previously-glazed pottery. The object was then placed into a kiln and heated to about 600 °C in a reducing atmosphere.

In the heat the glaze would soften, causing the copper and silver ions to migrate into the outer layers of the glaze. There the reducing atmosphere reduced the ions

back to metals, which then came together forming the nanoparticles that give the colour and optical effects.

Luster technique showed that ancient craftsmen had a rather sophisticated empirical knowledge of materials. The technique originated in the Islamic world. As Muslims were not allowed to use gold in artistic representations, they had to find a way to create a similar effect without using real gold. The solution they found was using luster.

Michael Faraday provided the first description, in scientific terms, of the optical properties of nanometer-scale metals in his classic 1857 paper. In a subsequent paper, the author (Turner) points out that: "It is well known that when thin leaves of gold or silver are mounted upon glass and heated to a temperature that is well below a red heat (~500 °C), a remarkable change of properties takes place, whereby the continuity of the metallic film is destroyed. The result is that white light is now freely transmitted, reflection is correspondingly diminished, while the electrical resistivity is enormously increased."

Challenges have been faced for lymphatic circulation [8]

The World Health Organization (WHO) Global Program to Eliminate Lymphatic Filariasisreliesonmass drug administration (MDA) of two drugs annually for 4 to 6 years. The goal is to reduce the reservoir of microfilariae in the blood to a level insufficient to maintain transmission by the mosquito vector. In 2008, the international medical aid organization Medecins Sans Frontieres (MSF) performed the first round of a MDA in the high-burden area of Asmat district, in Papua, Indonesia. We report the challenges faced in this MDA on a remote Indonesian island and propose solutions to overcome these hurdles in similar future contexts.

Lymphatic filariasis (LF) is a parasitic disease trans-mitted by mosquito bites which causes disability and adversely impacts the economy of the developing countries where it is endemic. LF is the fourth most common cause of disability worldwide. It is caused by Wuchereriabancrofti, Brugiamalayiothers. This MDA-based strategy of transmission inters, Brugiatimori. These parasites reside in lymphatic channels or lymphnodes where they remain viable for more than two dec-ades. W. Bancroftiis the most widely distributed, affect-ing an estimated 115 million people throughout the tropics and subtropics. The World Health Organization (WHO) estimates that 120 million people are currently infected and more than 1 billion people are at risk in 83countries. Approximately 40 million people are seriously incapacitated and disfigured by the disease. LF disease transmission can be stopped through a feasible, effective, and relatively inexpensive prevention strategy through mass drug administration (MDA) of two oral drugs to at-risk populations once a year. These drugs kill the microfilariae in an infected patient's blood so that mosquitoes cannot transmit the disease toruption is part of the WHO's Global Program to Eliminate Lymphatic Filariasis. Filariasis is an eradicable disease of high prevalence among several of the islands of Indonesia. Due to the high prevalence and remote distribution and diversity of filarial infections, filariasis elimination in Indonesia is a major challenge. In 2008, the international medical aid organization Medecins Sans Frontières (MSF) offered to carry out the first round of a MDA in the district of Asmat, Papua, Indonesia, where LF was found to be endemic. We report here our experience and the challenges faced in this MDA against LF in Asmat over an 11-week period.

Nano medicine current status and future prospects [9]

Applications of nanotechnology for treatment, diagnosis, monitoring, and control of biological systems has recently been referred to as "nanomedicine" by the National Institutes of Health. Research into the rational delivery and targeting of pharmaceutical, therapeutic, and diagnostic agents is at the forefront of projects in nanomedicine. These involve the identification of precise targets (cells and receptors) related to specific clinical conditions and choice of the appropriate nanocarriers to achieve the required responses while minimizing the side effects. Mononuclear phagocytes, dendritic cells, endothelial cells, and cancers (tumor cells, as well as tumor neovasculature) are key targets. Today, nanotechnology and nanoscience approaches to particle design and formulation are beginning to expand the market for many drugs and are forming the basis for a highly profitable niche within the industry, but some predicted benefits are hyped. This article will highlight rational approaches in design and surface engineering of nanoscale vehicles and entities for site-specific drug delivery and medical imaging after parenteral administration. Potential pitfalls or side effects associated with nanoparticles are also discussed.

CONCLUSION

Lymphatic system, a subsystem of the circulatory system in the vertebrate body that consists of a complex network of vessels tissues, and organs. The lymphatic system helps maintain fluid balance in the body by collecting excess fluid and particulate matter from tissues and depositing them in the bloodstream. It also helps defend the body against infection by supplying disease-fighting cells called lymphocytes. The lymphatic system can be thought of as a drainage system needed because, the blood circulates through the body, blood plasma leaks into tissues through the thin walls of the capillaries nanotechnology for treatment, diagnosis, monitoring, and control of biological systems. The use of Nanotechnology in medicine and more specifically drug delivery is set to spread rapidly. A conceptual understanding of biological responses to Lymphatic circulation by the help of nanotechnology is needed to develop more in the future.

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