Journal
J. Biol. Chem. Environ. Sci., 2010, Vol. 5(3): 595-608
www.acepsag.org

NANOTECHNOLOGY IN FOOD AND MEDICINE
(Review Article)

Emad S. Shaker

Agric. Chemistry Dept., Minia University, Minia, Egypt

ABSTRACT

Nanotechnology (NT) science defined as the extension of existing sciences into dimensional realms much smaller than previously considered feasible. While, Oberdorster *et al.*, (2005) declared that nanoscience and nanotechnology are the understanding and manipulation of materials at the atomic, molecular, and macromolecular scales. On another view, nanoscience involves research to discover new behaviors and properties of materials with dimensions at the nanoscale, which ranges roughly from 1 to 100 nanometers (nm), [1m=10^9nm, nm=$10A^{\circ}$]. So, nanotechnology is the way discoveries made at the nanoscale will put to work. Review will touch the various uses, benefits and cautions of nanotechnology science.

Introduction in the nanomaterial properties

Since nanotechnology deals with materials as small as a 1 billionth of a meter, began to enter into mainstream (Hodes, 2007) physical sciences 20 years ago. Recently, Nair *et al.* (2010) describes a gap of the low bioavailability of various nutraceuticals from fruits, vegetables and spices. This will limit their use in preventing lipid oxidation or treating diseases. Beside, their low solubility made them poorly absorbed by human body. They packaged several nutraceuticals as nanoparticles and proved to be useful in '*nanochemoprevention*' and '*nano-chemotherapy*'. Thus the most important and interesting applications for encapsulation of phytochemicals is to enhance their bioavailability.

Definitely, materials can behave different properties at the nanoscale. Some are better at conducting electricity or heat, some are stronger, some have different magnetic properties, and some reflect light better or change colors as their size is changed. Furthermore, nanoscale materials have far larger surface areas than similar volumes of larger scale materials. So that, more surface is available for interactions with other materials around them.

In this matter, gold is an excellent conductor of heat and electricity, but nothing much happens when we shine light onto a piece of gold. With properly structured gold nanoparticles start absorbing light and can turn that light into enough heat. Then, act like miniature thermal scalpels that can kill unwanted cells in the body, such as cancer cells.

Other materials can become remarkable strong when built at the nanoscale. For example, nanoscale tubes of carbon, 1/100,000 the diameter of a human hair, are incredibly strong. They are already being used to make bicycles, baseball bats, and some car parts. Scientists think they can combine carbon nanotubes with plastics to make composites that are far lighter, stronger than steel. Carbon nanotubes also conduct heat and electricity, so they could be used to protect airplanes from lightning strikes and to cool computer circuits.

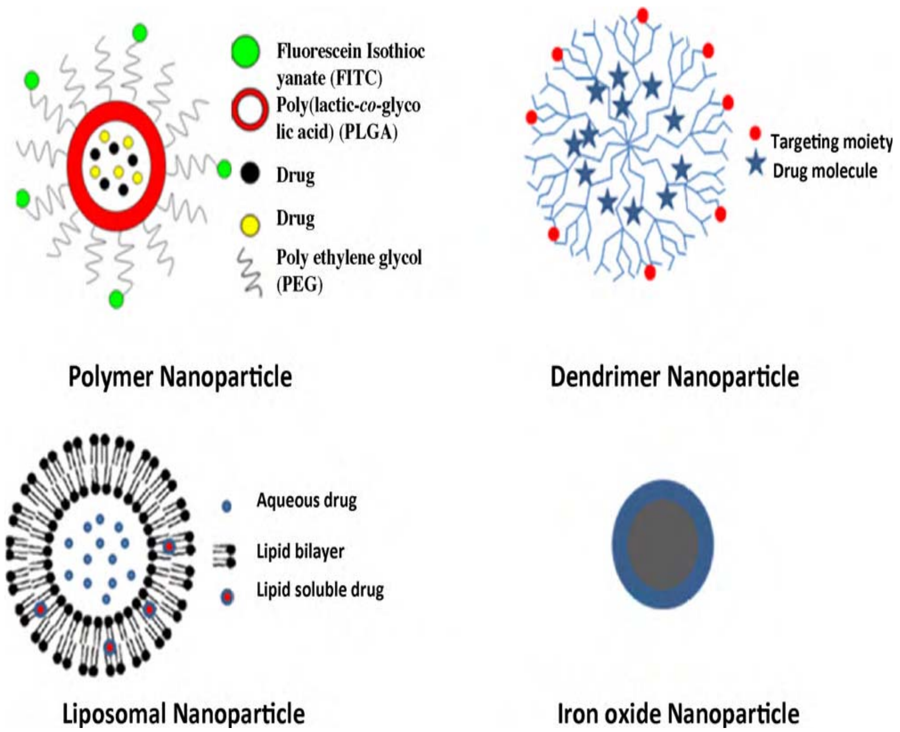
Current products using nanoscale materials and processes are now available. Antibacterial wound dressings use nanoscale silver. A nanoscale dry powder can neutralize gas and liquid toxins in chemical spills and elsewhere. Batteries for tools are being manufactured with nanoscale materials in order to deliver more power, more quickly, with less heat. Cosmetics and food producers are "nano-sizing" some ingredients, claiming that improves their effectiveness. Sunscreens containing nanoscale titanium dioxide or zinc oxide are transparent and reflect ultraviolet light to prevent sunburns. Scratch- and glare-resistant coatings are being applied to eye glasses, windows, and car mirrors.

There are many nanotechnology applications and products have been recently found. Nanoscale materials make *thin films* water-repellent, anti-reflective, self-cleaning, ultraviolet or infrared-resistant, anti-fog, anti-microbial, scratch-resistant or electrically conductive.

Nanotechnology in Medicine

The idea of controlled drug delivery has been shown to improve the therapeutic index of drugs by increasing their localization to specific tissues, organs or cells (Riehemann *et al.*, 2009). This approach tends to decrease potential side effects by leaving the normal sensitive cells unharmed (Ferrari, 2005). Nanoparticulate drug delivery systems using *liposomes* and *biodegradable polymers* have attracted increasing attention in recent years.

Dendrimers, virus nanoparticles and *magnetic nanoparticles* are types of nanostructure that can be precisely designed and manufactured for a wide variety of applications, including treatment of cancer and other diseases (Koning and Krijger, 2007). *Dendrimers* carrying different materials on their branches can do several things at one time, such as recognizing diseased cells, diagnosing disease states (including cell death), drug delivery, reporting location, and reporting outcomes of therapy. Kagan *et al.* (2005) mentioned that nanotechnology developments have led to *nanomedicine* with many diagnostic and therapeutic applications involving nanomaterials and nanodevices. It has been expected that nanomedical products will have a huge impact on public health care (Zajtchuk, 1999).

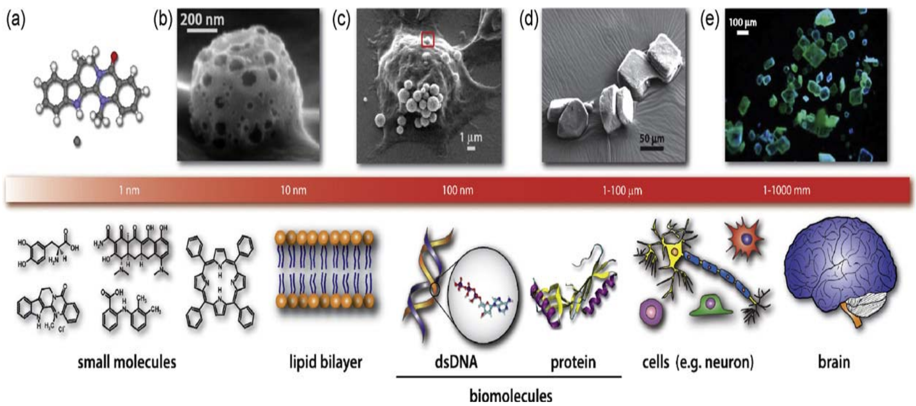


It has been recently interesting voice, that potential applications include toxicity reduction where the focus has been on decreasing drug concentration in overdose cases as the tricyclic antidepressants

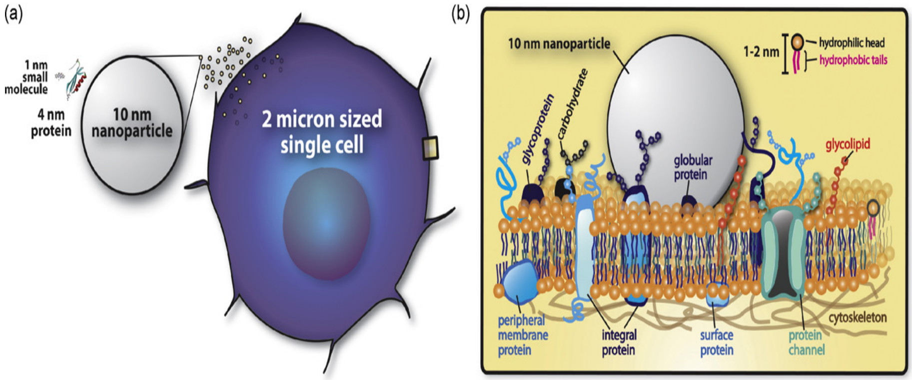
(Brucculeri *et al.,* 2005). Some approaches to *detoxification therapy* using nanopracticles and nanoemulsions (Morey *et al.,* 2004) have been demonstrated relative to their macro-scale counterparts. However, preparation of traditional Chinese medicine is comparatively low in nanotechnology application. That might be for two reasons; the modest cost and the low toxicity of the traditional Chinese medicine.

Nano-bio interface and nanotoxicology

Proteins and nucleic acids have been the focus of many types of research involving nanotechnology (Suh *et al*., 2009). A single cell, usually tens of microns in size, is huge compared to a 10 nm nanoparticle.



Researchers around the world have been utilizing various inorganic, organic and composite nanoparticles to study biological processes involced in drug delivery and cellular level bioimaging (Allen and Cullis, 2004). Recently, growing number of papers examine the interaction between a protein and a nanoparticle (Klein, 2007).



Compared to a 10 nm nanoparticle, the APP (amyloid precursor protein) and a small drug molecule (e.g. DHED; dehydroevodiamine hydrochloride) is extremely small which makes probing biologically relevant molecules on nanoparticles extremely difficult. An injected nanoparticle into a living system will have an uncountable number of interactions with the surrounding system regardless to size. Studying the interface between nanostructured materials (proteins) and biological systems (cell) will be a key development in neuroscience, pharmacology and medicine.

Nantoechnology in Agro-production

Increase the efficacy of the agro-chemicals is the aim of using nano-formulated in the conventional formulation. Only some pesticides containing nano-sized or nano-formulated agro-chemicals were identified in market. However, residues of these products might be present in products as consumed. Other applications for nano-particles NPs are the water and soil cleaning purposes such as; aluminium oxide, lanthanum particles and nanoscale iron powder.

On the other side, as *global climate problems* increasingly draw attention to environmental issues, interest in natural solutions has also grown. Since most of the important plant materials used in traditional Chinese medicine are cultivated in regions that attract environmental concerns. Large scale harvest of the raw plant materials causes more and more serious environmental problems as dust storms. Application of nanotechnology to commonly used traditional medicine plant materials may not only improve their bioactivity but also reduce the amount of the nanopharmaceuticals required and decrease environmental degradation associated with the harvesting of the raw products.

Nanotechnology in Food Industry

Increasing interest in discovering *natural antioxidants* derived from traditional medicines as it is believed that they protect the human body from the attack of free radicals and retard the progress of many chronic diseases (Pryor, 1991). Natural antioxidants are likely to be more desirable than chemically produced analogs because some of the latter are reportedly carcinogenic (Imaida *et al.,* 1983). The antioxidant activities of medicinal plant materials prepared using nanotechnology method (Liu *et al.,* 2008). They indicated that the polar active constituent in the nanotechnology samples was released faster compared to the traditionally powdered samples.

Dry nanoparticles were produced from grounding plant materials using atomizer and sprayed granulating with the aid of floating bed. Transmission Electron Microscopy (TEM) certified the particle size in the nanoscale range. TEM was achieved by adding 1-dodecane in major oil as a dopant to the nanocapsule oil core. The emerging technology has shown great potential in *nutraceuticals and functional foods* for delivering bioactive compounds in functional foods to improve human health (Chen *et al.,* 2006).

Some researchers are working toward nano-manufacturing and a “bottom-up” approach to making things. The idea is that if you can put certain molecules together, they will self assemble into ordered structures. This approach could reduce the waste of current”top-down” manufacturing processes that start with large pieces of materials and end with the disposal of excess materials.

Owning to the lack of information about the impacts of nanotechnology on public safety, legislation, society, and food industry as well as the potential toxicity of nanomaterials, it is probably wise to take a precautionary principle to deliberate the possible regulatory control as a proactive approach until proven otherwise. In the same time, we will not avoid the worldwide sales of nanotechnology products jumped from US$ 150 million in 2002 to expected US$ 20.4 billion in 2010 (Fletcher, 2006).

Champagne and Fustier (2007) found that Microencapsulation (ME) is a useful tool to improve the delivery of bioactive compounds into foods, particularly probiotics, minerals, vitamins, phytosterols, lutein, fatty acids, lycopene and antioxidants. These technologies could promote the successful delivery of bioactive ingredients to the gastrointestinal GI tract. ME has been defined as the technology of packaging solid, liquid and gaseous materials in small capsules that release their contents at controlled rates over prolonged periods of time. Such technologies are of significant interest to the pharmacutical sector (drug and vaccine delivery), and food industry.

Uptake of nanoparticles in GI tract depends on diffusion and accessibility through mucus, initial contact with the gut epithelium and translocation processes. The diffusion rate also depends on the charge of the particle; anionic particles have been shown to reach the epithelial surface, whereas cationic particles were traped in the mucus (Szentkuti, 1997). The mucus layer can thus be considered the first barrier NPs have to pass before entering the body. Once nano-encapsulates pass the GI epithelium and end up in the blood circulation, they can interact with various blood-components depending on the surface chemistry of the particle (Nemmar *et al.,* 2002).

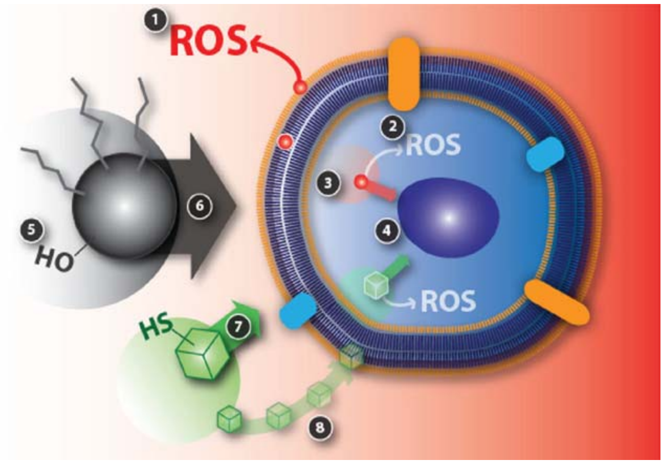
The hydrophobic surfaces of nanospheres are highly susceptible to opsonization and clearance by the reticulo-endothelial system, resulting in sequestering of the particles within organs such as the liver and spleen (Letchford and Burt, 2007). The smallest NPs revealed a more diverse distribution to e.g., brain, bone marrow, spleen and liver (De Jong *et al.,* 2008).

Probiotic bacteria are defined, live microorganisms which administered in adequate amounts, showing a beneficial physiological effect on the host. The ME size should be between 1 and 5 µm diameter, and they must be kept alive. Some ME methods are suitable as spray-coating, spray-drying, extrusion, emulsion and gel particle technology.

Cell-nanoparticle interface

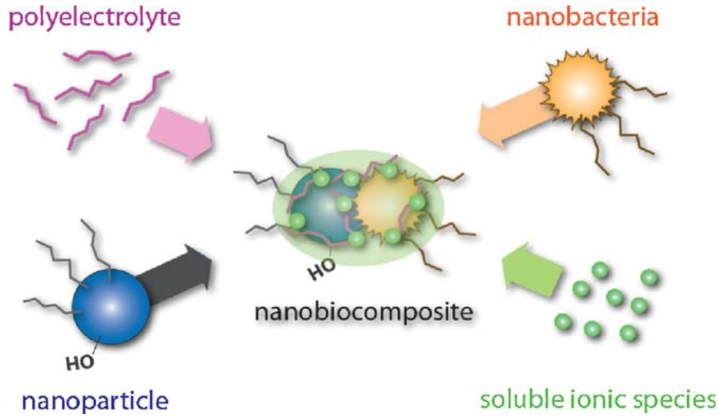
Expanding the toxicity studies to mammals should be done but since it is practically impossible to test on a human subject it will be difficult to assess nanomaterials' effects on human beings with just animal studies alone. Nanostructured materials will be in contact with some biologically relevant entity once it enters a biological system. This makes any biochemical assay or structural analysis irrelevant just on its own.

Biological effects of nanomaterials with a focus on toxicity have to be addressed since consumer products as well as medical tools increasingly utilize them one way or another (Maynard *et al.*, 2006). Cellular organism can be affected in this field by a nanoparticle (the cell nanoparticle interface).



Reactive oxygen species (ROS) products whether it is inside or outside of the cell can be key factors in nanostructured materials toxicological effects (Nel *et al.*, 2006). Nnanoparticle (ROS) will ultimately affect cell membrane stability, and cell survivability. If this nanoparticle is internalized, ROS production, particle dissolution, and mechanical damage will occur to sub-cellular units such as the nucleus. Different functional groups and surface electronics of the nanostructured materials will determine the level of interaction between the nanoparticles and their surroundings (Kostarelos *et al.*, 2007).

Oversize of the particle can play an important role since large particles can potentially induce permanent damage to the cell membrane while small particles can pass through the membrane and do harm inside the cell. Non-spherical particles might have a different biological response compared to the spherical nanoparticles (Geng *et al.*, 2007). Dissolution of the nanomaterials can affect the cell in various ways, as in the figure.



Beside these nantoxicology events, nanomaterials interaction with microbial organisms (Moreau *et al.,* 2007) will be an interesting aspect to consider, since biologically contaminated nanostructured materials will have detrimental effects on their utilization in biomedical applications. For instance, mycoplasmas have a size range below few hundred nanometers and they have become a rising concern in mammalian cell cultures including stem cells (Simonetti *et al.,* 2007).

If such microbial organisms integrate themselves readily with engineered nanomaterials, their toxic potential as a nanocomposite material could increase. Toxicology arising from such nanobiocomposites will give new meaning to nanotoxicology. Since mycoplasma detection is not trivial, neuroscientists use nanotechnology with focuses on neuronal cell systems, brain implantations and dementia research such as Alzheimer's disease (Casserly *et al.,* 2007).

Cautions for spread using of NT

Chau *et al.* (2007) illustrated the entry of the small size nanoparticles into body and the translocation among organs. Possible routes for nanoparticles to cause harm inside the body include dermal exposure, inhalation, or ingestion. Stringent control on exposure should be implemented for the limited information on the risks of handling nanomaterials. Lab safety guidelines have been provided by the Committee on Chemical Safety of the American Chemical Society. Penetration into skin, interaction with the immune system, and the photogeneration of hydroxyl radicals by nanomaterials could lead to oxidative damage in the skin (Wakefield *et al.,* 2004). Also, when inhaled some nanoparticles may accumulate in the lung and induce chronic diseases such as pulmonary inflammation, pneumonia, pulmonary granuloma, and oxidative stress (Nel *et al.,* 2006). In addition, direct ingestion of nanomaterials through food, water, cosmetics, or drugs, and those cleared *via* the mucociliary escalator in the respiratory tract can end up in the gastrointestinal tract (Nel *et al.,* 2006).

Knowledge on the potential toxicity of NPs is limited, but rapidly growing. Test animals are generally exposed to high concentrations under artificial conditions. So, there is too few data to determine which type of effects are to be expected for which type or size of NP. Numerous in vitro studies using various NPs are being published (Donaldson and Seaton, 2007). Acute oral toxicity at high doses of NPs (e.g., copper, selenium, zinc and zinc-oxide and titanium dioxide) may occur depending on the particle size, coating and chemical composition (Wang *et al.,* 2008).

Effects on the immune and inflammatory systems may include oxidative stress and /or activation of pro-inflammatory cytokines in the lungs, liver, heart and brain. Genotoxicity and possible carcinogenesis may also occur. NP may pass the blood-brain barrier following systemic availability (Silva, 2007). Clearly, that needs collaborations between NP developers, risk assessors, regulators and researchers.

It is undoubted that the application of nanotechnology in food (called nanofood or ultrafine food) and packaging is growing rapidly. Currently, there is still no requirement to label food products containing nanoparticles and no regulatory standard to comply with. Moreover, Scientists comparing between challenges facing nanotechnology with that facing genetically modified (GM) foods into industries and markets.

National Nanotechnology Initiative (NNI) agencies invest in fundamental research to further understanding of nanoscale phenomena. Manufacturers are responsible for the safety of their products; however, U.S. Government regulatory agencies such as; Environmental Protection Abency (EPA) and Food and Drug Administration (FDA) are responsible for protecting public health and the environment through regulation.

REFERENCES

Allen, T. and Cullis, P. (2004) Drug delivery systems: entering the mainstream. Sci. 303, 1818-1822.

Brucculeri, M.; Kaplan, J. and Lande, L. (2005) Reversal of citalopram-induced junctional bradycardia with intravenous sodium bicarbonate. Pharmacotherapy, 25, 119-122.

Casserly, G.; Barry, T.; Tourtellotte, W. and Hogan, E. (2007) Absence of mycoplasma-specific DNA sequence in brain, blood and CSF of patients with multiple sclerosis (MS): a study by PCR and real-time PCR. J. Neurol. Sci. 253, 48-52.

Champagne, C. and Fustier, P. (2007) Microencapsulation for the improved delivery of bioactive compounds into foods. Current Opinion in Biotechnol. 18, 184-190.

Chau, C.; Wu, S. and Yen, G. (2007) The development of regulations for food nanotechnology. Trends in Food Sci. Technol. 18, 269-280.

Chen, H.; Weiss, J. and Shahidi, F. (2006) Nanotechnology in nutraceuticals and functional foods. Food Technol. 3, 30-36.

De Jong, W.; Hagens, W.; Krystek, P.; Burger, M.; Sips, A. and Geertsma, R. (2008) Particle size-dependent organ distribution of gold nanoparticles after intravenous administration. Biomaterials. 29, 1912-1919.

Donaldson, K. and Seaton, A. (2007) The Janus faces of nanoparticles. J. Nanosci. Nanotechnol. 7, 4607-4611.

Ferrari, M. (2005) Cancer nanotechnology: Opportunities and challenges. Nat. Rev. Cancer. 5, 161-171.

Fletcher, A. (2006) Nanotech food conference targets future opportunities. Available from http://www.foodnavigator.com/news/ng.asp?id=67113.

Geng, Y.; Dalhaimer, P.; Cai, S.; Tsai, R.; Tewari, M.; Minko, T. and Discher, D. (2007) Shape effects of filaments versus spherical particles in flow and drug delivery. Nat. Nanotechnol. 2, 249-255.

Hodes, G. (2007) When small is different: some recent advances in concepts and applications of nanoscale phenomena. Adv. Mater. 19, 639-655.

Imaida, K.; Fukushima, T.; Shivai, T.; Ohtani, M.; Nakanishi, K. and Ito, N. (1983) Promoting activities of butylated hydroxyanisole and butylated hydroxytoluene on 2-stage urinary bladder carcinogenesis and imhibition of -glutamyl transpeptidase-positive foci development in the liver of rats. Carcinogenesis, 4, 895-899.

Kagan, V.; Bayir, H. and Shvedova, A. (2005) Nanomedicine and nanotoxicology: two sides of the same coin. Nanomed. Nanotechnol. Biol. Med., 1, 313-316.

Klein, J. (2007) Probing the interactions of proteins and nanoparticles. Proc. Natl. Acad. Sci. USA 104, 2029-2030.

Koning, G. and Krijger, G (2007) Targeted multifunctional lipid-based nanocarriers for image-guided drug delivery. Anticancer Agents Med. Chem. 7, 425-440.

Kostarelos, K.; Lacerda, L.; Pastorin, G.; Wu, W.; Wieckowski, S.; Luangsivilay, J.; Godefroy, S.; Pantarotto, D.; Briand, J.; Muller, S.; Prato, M. and Bianco, A. (2007) Cellular uptake of functionalized carbon nanotubes is independent of functional group and cell type. Nat. Nanotechnol. 2, 108-113.

Letchford, K. and Burt, H. (2007) A review of the formation and classification of amphiphilic block copolymer nanoparticulate structures: micelles, nanospheres, nanocapsules and polymersomes. Eur. J. Pharm. Biopharm. 65, 259-269.

Liu, J.; Chen, G.; Shih, H. and Kuo, P. (2008) Enhanced antioxidant bioactivity of *Salvia miltiorrhiza* (Danshen) products prepared using nanotechnology. Phytomedicine, 15, 23-30.

Maynard, A.; Aitken, R.; Butz, T.; Colvin, V.; Donaldson, K. and Oberdorster, G. (2006) Safe handling of nanotechnology. Nature. 444, 267-269.

Moreau, J.; Weber, P.; Martin, M.; Gilbert, B.; Hutcheon, I. and Banfield, J. (2007) Extracellular proteins limit the dispersal of biogenic nanoparticles. Sci. 316, 1600-1603.

Morey, T.; Varshney, M.; Flint, J.; Rajasekaran, S.; Shah, D. and Dennis, D. (2004) Treatment of local anesthetic-induced cardiotoxicity using drug scavenging nanoparticles. Nano Lett. 4, 757-759.

Nair, H.; Sung, B.; Yadav, V.; Kannappan, R.; Chaturvedi, M. and Aggarwal, B. (2010) Delivery of anti-inflammatory nutraceuticals by nanoparticles for the prevention and treatment of cancer. Biochem. Pharmacol. In Press

Nel, A.; Xia, T.; Madler, L. and Li, N. (2006) Toxic potential of materials at the nanolevel. Sci. 311, 622-627.

Nemmar, A.; Hoet, P.; Vanquickenborne, B.; Dinsdalem, D.; Thomeer, M. and Hoylaerts, M. (2002) Passage of inhaled particles into the blood circulation in humans. Circulation, 105, 411-414.

Oberdorster, G.; Maynard, A.; Donaldson, K.; Castranova, V.; Fitzpatrick, J.; Ausman, K.; Carter, J.; Karn, B.; Kreyling, W. and Lai, D. (2005) Principles for characterizing the potential human health effects from exposure to nanomaterials: elements of a screening strategy. Particle and Fibre Toxicology. 2, 8.

Pryor, W. (1991) The antioxidant nutrients and disease prevention – what do we know and what do we need to find out? Am. J. Clin. Nutr. 53, S391-S393.

Riehemann, K.; Schneider, S.; Luger, T.; Godin, B.; Ferrari, M. and Fuchs, H. (2009) Angew Chem. Int. Ed Engl. 48, 872-897.

Silva, G. (2007) Nanotechnology approaches for drug and small molecule delivery across the blood-brain barrier. Surgical Neurology. 67, 113-116.

Simonetti, A.; Englert, G.; Campos, K.; Mergener, M.; de David, C.; de Oliveira, A. and Roche, P. (2007) Nanobacteria-like particles: a threat to cell cultures. Braz. J. Microbiol. 38, 153-158.

Suh, W.; Suslick, K.; Stucky, G. and Suh, Y. (2009) Nanotechnology, nanotoxicology, and neuroscience. Progress in Neurobiol. 87, 133-170.

Szentkuti, L. (1997) Light microscopical observations on luminally administered dyes, dextrans, nanospheres and microspheres in the pre-epithelial mucus gel layer of the rat distal colon. J. Controlled Release. 46, 233-242.

Wakefield, G.; Green, M.; Lipscomb, S. and Flutter, B. (2004) Modified titania nanomaterials for sunscreen applications – reducing free radical generation and DNA damage. Materials Sci. Technol. 20, 985-988.

Wang, Y.; Li, Y.; Wang, Q. and Fang, X. (2008) Pharmacokinetics and biodistribution of polymeric micelles of paclitaxel with pluronic P105/poly (caprolactone) copolymers, Pharmazie. 63, 446-452.

Zajtchuk, R. (1999) New technologies in medicine: biotechnology and nanotechnology. Disease-a-Month 45, 453-495.

علم النانوتكنولوجى فى الغذاء والطب

عماد صبرى شاكر

قسم الكيمياء الزراعية – جامعة المنيا – المنيا – مصر

يعرف علم النانوتكنولوجى –فى عدة دراسات- بأنه أمتداد للعلوم المهتمة بالمواد المتواجدة فى أبعاد دقيقة جدا وأصغر من أن ترى بالعين المجردة. بينما أعلن العالم أبردرستر واخرون (2005) بأن علوم النانو وعلوم النانوتكنولوجى هى فهم وتفسير لسلوك المواد فى حالتها الذرية والجزيئية وجزئيات الماكرو. ومن جهة أخرى تشمل أبحاث النانو أكتشاف سلوك وخواص جديدة للمواد ذات الأبعاد بقياس النانو فى مدى 1 – 100 نانومتر (المتر = 10^9 نانومتر، والنانومتر = 10 أنجســــتروم). ويمكن القول بأن علم النانوتكنولوجى هو طريقة أكتشاف جديدة على مدى قياس النانو. وهذا البحث المرجعى يلمس أستعمالات عديدة لهذا العلم وفوائد ومحازير لهذا العلم الحديث.