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Review

Nanotechnology: A non-invasive diagnosis and therapeutic tool for brain disorders

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Presently, nanotechnology appears as a powerful and innovative tool in the medical field. It has various advantages over the conventional drug therapy such as therapeutic specificity, has less side effects, reduces dose of drug, has more precise treatment and can access the inaccessible areas of the body like brain, tumor cells, etc. The human brain is the most complicated part of the body which is highly protected with the blood-brain barrier (BBB) and the other protective measures of the body. The available treatments for brain disorder are highly invasive (parenteral or surgical procedures) in nature or cause high peripheral toxicity (oral administration). Thus, a prominent strategy is needed which can easily approach the brain and offers a more specific treatment. Nanomedicines are effective tools used for the diagnosis and treatment of brain disorders.

Key words: Brain, neurodegenerative disorders, nanotechnology, gold nanoparticle, quantum dots.

INTRODUCTION

The brain is the most delicate, complex and vital organ of the human body. It regulates all the responses and stores information (Sonali et al., 2018). Our brain makes us feel, sense and be aware of every little sense and stimulusoutside as well as inside the body.The body has its protective measures to shield the brain from any

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damage. Among these, the very first protective structure is the skull which covers the whole brain and protects it from external injuries. The other primary protective layers include the meninges, blood-brain barrier (BBB) and blood-cerebrospinal fluid barrier (Tsou et al., 2017). Throughout life, our brain comes in contact with various types of stimuli which sometimes harm the integrity and function of brain. The brain disorders may vary from accidental injury, shock, trauma, stroke from poisoning, infection, physiological dysfunctioning, genetic disorders, aging, etc. which damage any particular part or group of neurons (Orive et al., 2009). Concerning the treatment of brain disorder, medical science still has not any answer to brain disorders. There are some factors associated with brain physiology which restrict the therapy. A significant factor is the presence of physiological barriers like BBB which limits the entry of almost all the external molecules (including drug and nutrients) to the brain. Such protective feature makes the brain inaccessible to the drug and diagnostic aids (Blanco et al., 2015). Hence, the treatment needs a large dose of the drug to attain the therapeutic level that causes a systemic side effect. Along with this, the other treatment strategy includes surgical procedures or intracerebroventricular injections, a highly invasive and painful approach (Silva Adaya et al., 2017).

Considering such challenges, researchers are continuously trying to find out a promising and convenient tool to deliver the drug to the brain without interfering with the efficacy of the drug. One such approach is nanotechnology, the engineered nano-sized tools that regulate and manipulate the physicochemical prospects of any material or device at the molecular level (Huang et al., 2017). Research proves that nanotechnology is a useful tool that can replace or improve the presently available drug therapies and modify the diagnostic aids by using molecular imaging and modeling (Fan and Yeh, 2014; Silva et al., 2017; Sonali et al., 2018). The nanotherapeutics utilize various nanocarrier systems like liposome, nanoparticle, nanogels, dendrimer, nanotube, nanofiber, etc. and different targeting strategies to enhance the specificity of the treatment (Saraiva et al., 2016; Agrawal et al., 2017; Tsou et al., 2017; Poupot and Bergozza, 2018). The significant advantage of nanotechnology firstly involves its ability to deliver the drug across the BBB (Blanco et al., 2015), owing to the smaller size, secondly, the controlled and sustained release behavior (Saraf et al., 2015), thirdly, the targeting ability and lastly the ability to protect the drug integrity (Silva Adaya et al., 2017). Along with this, nanocarriers are highly stable, able to carry both the lipophilic and hydrophilic molecules and biodegradable in nature (Alexander et al., 2016; Kumar et al., 2017). This behavior makes nanocarrier a suitable tool for accessing the brain (Hassanzadeh et al., 2017). This novel technology is not only limited to the oral and parenteral administration, but it can also be given through topical, transdermal and intranasal route to the brain. By this way, it offers a non-invasive treatment over the painful parenteral and highly invasive surgical measures.

ADVANCED NANO-TOOLS

For the effective treatment and diagnosis of brain disorders, some advanced form of nanomaterials is presently under investigation like gold nanoparticle, carbon nanotube, a magnetic nanoparticle, silicon nanowires, etc.

Silicon nanowires

Silicon nanowires are a semiconductor nanowire made of silicon precursors. These are quasi-1D structures with a size of approximately 100 nm. The small size of the nanowires offers a larger surface area. Its unique mechanical, optical and electronic properties, biocompatibility and low toxicity profile makes it a promising therapeutic and diagnostic tool. Moreover, owing to the high surface-volume ratio, the silicon nanowires are used in biotechnology, for development of nanosensor, high-performance silicon nanoprobes, nanowires, etc. for biological investigation and recognition and treatment of various brain disorders (Peng et al., 2014). Also, the fluorescence silicon nanowires can be used for identification and imaging of tumor or cancer cells, detection of plaque formation, and recognition of DNA and proteins. Parmeshwaran et al. (2018) have developed a photosensitive silicone nanowire to modulate the neuronal activity and regulate cellular excitability in a non-genetic and non-invasive manner. The nanowires are administered in a drug like fashion and get activated inside the body by absorbing light (Lanzani, 2018). The study shows the nanotool as an effective and alternative approach over highly invasive surgical procedures for the treatment of brain disorders (Parameswaran et al., 2018).

Gold nanoparticle

Another important strategy is the gold nanoparticle which is now popular in neuroscience. These are nanosized colloidal particles made of gold, having a size of less than 100 nm and offer multiple surface functionalization (Kerdi et al., 2010). Due to the high surface functionality, it can easily interact with different antibiotics, proteins and oligonucleotides, thus, can serve as a promising diagnostic tool. It can also bind with targeting ligands and can cargo various drug substances, hence, used as a potential drug carrier (Brown et al., 2010). These are the potential oxidizing catalyst of liquid and gases. Thus, a suitable stabilizer or chemical method is needed to stabilize nanoparticles (Kerdi et al., 2010). It offers various advantages like drug targeting, cell signaling, nerve modulation, and signaling, etc. The application of gold nanoparticle in the treatment of neurological disorders includes neuro suppression (Yoo et al., 2014), nerve depolarization (Eom et al., 2014; Yong et al., 2014), neuromodulation by interfering with intracellular calcium signaling (Paviolo et al., 2014; Nakatsuji et al., 2015), neurite outgrowth enhancement (Paviolo et al., 2013; Papastefanaki et al., 2015). Along with this, gold nanoparticles are also used for gene therapy (Paviolo and Stoddart, 2017)

Carbon nanotubes

Carbon nanotubes were firstly prepared by Sumio Iijima in 1991, from the arc discharge of graphite electrode in an experiment (Iijima, 1991). The carbon nanotubes are entirely made of carbon atoms, arranged as a benzene ring; these benzene ring-like structures are made as graphene sheet which further turns into a cylindrical shape. By the arrangement, the carbon nanotubes are of two types (i) single-walled carbon nanotube and (ii) multi-walled carbon nanotube. The single-walled carbon nanotube consists of a single graphene sheet and having a cylinder diameter of less than 2.5 nm; while the multi-walled carbon nanotube is made of 2 or more graphene sheets with a cylindrical diameter up to 100 nm (Silva Adaya et al., 2017). The unique structure of the carbon nanotube is attributed to the high tensile strength, semiconductor property, high thermal conductivity, sustainability to the high current density, high resilience, etc. Thus it can be used as scanning probes, nanosensors, gas sensors and various nano-electric devices for bioanalysis (Esawi and Farag, 2007). The carbon nanotubes possess excellent plasma membrane permeability (Pantarotto et al., 2004), high drug loading, intrinsic spectroscopic behavior, hence, found suitable in disease diagnosis, imaging, and application in biotechnology (Lin et al., 2004). Recently it is also proposed as a component of protein biosensor, DNA (Li et al., 2005; Allen et al., 2007) and as ion channel blocker (Manish et al., 2005).

Super paramagnetic iron oxide nanoparticles (SPIONs)

Owing to the unique magnetic behavior, the SPIONs can serve as a promising diagnostic and therapeutic tool for CNS disorders. Their magnetic properties and surface modification assist in the identification of tumor cells, lesions and other pathological factors of CNS disorders. At the same time, they can be used as a potential drug carrier system which specifically delivers the drug to its target site (Krupa et al., 2014). The main advantage and sometimes limitation of the magnetic nanoparticle is the necessity of an external magnetic field. The SPIONs get activated by the application of an external magnetic field and are inactive in its absence. Such property offers a great control over drug release, targeting and imaging responses of SPION. The average size of the magnetic nanoparticle is approximately 100 nm (SPION), and the particles with size less than 50 nm are known as ultra-super paramagnetic iron oxide nanoparticle (USPION) (Corot et al., 2006; Lodhia et al., 2010). In the past decade, the USPION became more popular as diagnostic agent than the SPION due to its unique ability to be visualized in both T1-MRI sequence and T2-MRI sequence as hyperintense (bright) and hypointense (dark) signal, respectively (Bridot et al., 2007; Na et al., 2007; Pan et al., 2008). Due to its smaller size, USPION can be absorbed by tumor cells via phagocytosis. However, the surface modification with an antibody or specific ligands could increase the targeting efficiency (Hadjipanayis et al., 2010). In addition, the USPION is a more patient-friendly carrier system with very less or no renal side effects (Neuwelt et al., 2007; Neuwelt et al., 2009).

Quantum dots

Quantum dots are one of the most studies nanotools nowadays. These are nano-sized crystalline colloidal semiconductor materials commonly consist of metallic crystals like selenium, cadmium, etc. At the core, they are enclosed by inert metal shell like zinc sulfide. These are the inorganic nanomaterials with high brightness, greater photostability and easy tunability to the narrow emission spectra. Such properties make them a promising diagnostic and therapeutic tool (Li et al., 2017). They are broadly used in biolabelling, biosensors, lasers, light emitting diodes and in the medical field for diagnosis as well as in therapy. In general quantum dots are fluorescent nanocrystals made of semiconductor materials which continuously emit energy. Because of the light emission property, quantum dots are found very useful in biological diagnosis and imaging (Silva Adaya et al., 2017).

Nanotechnology generally deals with the formulation of nano-sized particles or carrier system used for delivery of drug to treat various diseases. The NIH (National Institute of Health) of USA approved nanomedicines for diagnostic and therapeutic application (Markman et al., 2013). The nanocarriers have great advantages over conventional therapies and diagnosis techniques. They are easy to prepare by adopting standard techniques, can provide target specific action or recognition by surface functionalization with specific ligands. Moreover, the radiolabelled or fluorescent probes or other nano-sized devices offer a significant degree of monitoring and produce more precise results (Sonali et al., 2018). Also, they are biocompatible and can be used as a component of various biotechnological devices, DNA, protein and can offer ease of permeation across the biological membranes like BBB. The radiolabelled nanoparticles, nanoprobes, magnetic nanoparticle, gold nanoparticle, photoresponsive nanomaterials, surface modified (with a biomarker, ligand or specific antibody) nanoparticle represent an efficient and non-invasive method of diagnosis (Viola et al., 2015). However, their application is limited due to their toxicity profile and unpredictable *in vivo* response of these devices.

INTRANASAL APPROACH AS AN ALTERNATIVE ROUTE FOR BRAIN DRUG DELIVERY

One more interesting strategy is the nose-to-brain delivery of nanoparticle. The intranasal route directly delivers the drug to the brain through the olfactory route and bypasses the BBB. By this way, it enhances the drug efficacy, brain targeting and reduces the dose of the drug and systemic side effect. The amalgamation of nanotechnology with the intranasal route improves the retention time of drug in the nasal cavity, protects the drug from enzymatic degradation and target the drug to a particular part of the brain. Hence, the delivery of nanomedicines via nasal route offers an attractive, non-invasive and cost-effective therapy for brain disorders (Sonvico et al., 2018).

CONCLUSION

In this work, we have discussed a few examples of nanotools used as a diagnostic and therapeutic tool for brain disorders. There are a wide number of different nanotechnological approaches available for application or under research which overcomes the limitation of the conventional medical system. It offers a very convenient, more precise and quality services in the healthcare system. Although. some pitfalls are also there like the toxicity profile of nanomedicines which restricts the clinical application of such a prominent tool. Some of the nanomedicines were approved by the FDA for commercial application as anti-cancer drugs, analgesic agents and many more. Although, most of the works are in the pipeline. On the basis of the extensively successful research attempts, we the evidence of nanotechnology will be the next era of medical science.

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CONFLICT OF INTERESTS

The authors have not declared any conflict of interests.

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