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THERAPEUTICS POTENTIAL OF POLYSACCHARIDE BASED NANOCARRIERS: A REVIEW

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ABSTRACT

Polysaccharide-based nanoparticles have garnered significant attention in recent years due to their unique properties and diverse applications in the biomedical field. These nanoparticles are fabricated from natural polysaccharides, such as chitosan, alginate, cellulose, starch, and hyaluronic acid, which offer inherent biocompatibility, biodegradability, and low toxicity, making them attractive candidates for drug delivery, imaging, and tissue engineering. This abstract provides a comprehensive overview of the synthesis, properties, and biomedical applications of polysaccharide-based nanoparticles. The synthesis methods encompass both chemical and physical approaches, including emulsification, nanoprecipitation, ionic gelation, and self-assembly techniques. These methods allow for precise control over nanoparticle size, shape, and surface characteristics, which directly impact their functionality and performance in various applications. Furthermore, polysaccharide-based nanoparticles find utility in medical imaging, providing contrast agents for enhanced diagnostic accuracy and disease monitoring. Additionally, they hold immense potential in tissue engineering, facilitating scaffold fabrication and promoting tissue regeneration through controlled release of growth factors and bioactive molecules.
***Keywords*:** Polysaccharide, nanoparticles, biocompatibility, toxicities,

Introduction

Polysaccharide-based nanoparticles are a type of biomaterial that has gained increasing attention in the field of nanotechnology. These nanoparticles are composed of natural and synthetic polysaccharides that have been modified to form nanoparticles with unique properties, making them suitable for various applications in drug delivery, imaging, and tissue engineering. (William *et al.*, 2021) applications for polysaccharides based nano particles in below table 1.

Table 1: Applications of polysaccharides based Nanoparticles

Application of polysaccharides based nano particles	Biomedical and biotechnical applications	Gene delivery, Drug delivery Tissue engineering, Cancer therapy, Biosensors, Coating
	Agro- based applications	Controlled release of pesticides Water storage granules
	Industrial application	Cosmetics Preservatives, Chromatography Waste water treatment, Corrosion resistant Electrophoresis

Polysaccharides are long chains of sugar molecules that are commonly found in nature, including in plants, animals, and microorganisms (Jessica *et al.*, 2021). These molecules can be extracted and modified to create nanoparticles with specific characteristics such as size, shape, and surface charge, which can be tailored for various applications.

Overview of the polysaccharide Nano particles Formation and their applications show in Fig. 1 (Kyota Kamamoto *et al.*, 2021).

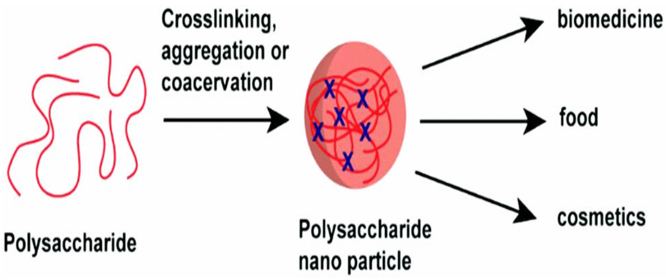

Fig. 1 : Formation of Nano polysaccharides by Cross linking

Types of polysaccharides-based Nano particles

There are several types of polysaccharide-based nanoparticles that have been developed and characterized for various biomedical applications (Jessica *et al*., 2021) These include:

Chitosan nanoparticles

Chitosan is a natural polysaccharide derived from chitin, which is found in the exoskeletons of crustaceans such as shrimp and crab (Kyota Kamamoto, Akihito Kiyama *et al*., 2021). Chitosan nanoparticles have a positive surface charge, which allows them to interact with negatively charged cell membranes and facilitate cellular uptake (Hua Zhang *et al*., 2019). They have been extensively studied for drug delivery, gene delivery, and imaging applications (Miaosi Li *et al*., 2018).

Alginate nanoparticles

Alginate is a natural polysaccharide extracted from brown seaweed, which has been modified to form nanoparticles with a negative surface charge (Jiaxiu Wang, Kai Zhang 2018). Alginate nanoparticles have been investigated for drug delivery and tissue engineering applications due to their biocompatibility and ability to form hydrogels in the presence of divalent cations (Fernando Jativa and Xuehua Zhang, 2017).

Starch nanoparticles

Starch is a natural polysaccharide found in many plant-based foods such as potatoes, rice, and corn (Jessica E.B. *et al*., 2021) Starch nanoparticles have been developed for drug delivery and imaging applications due to their biodegradability, biocompatibility, and ability to form stable colloidal suspensions (Xingjuan Zhao *et al*., 2016).

Dextran nanoparticles

Dextran is a natural polysaccharide derived from bacteria that has been modified to form nanoparticles with a neutral surface charge (Shih-Jiuan *et al*., 2016). Dextran nanoparticles have been investigated for drug delivery and imaging applications due to their biocompatibility, ability to form stable colloidal suspensions, and ability to be easily functionalized with targeting moieties (Ziyang Lu, Haolan Xu *et al*., 2015).

Hyaluronic acid nanoparticles

Hyaluronic acid is a natural polysaccharide found in the extracellular matrix of many tissues, which has been modified to form nanoparticles with a negative surface charge (Jessica *et al*., 2021). Hyaluronic acid nanoparticles have been investigated for drug delivery and imaging applications due to their biocompatibility, ability to target cancer cells that over express the CD44 receptor, and ability to enhance drug retention in tumour tissues (Shuhua Peng *et al*., 2014).

The schematic illustration depicts the formation of nanoparticles using two polysaccharide-based materials, namely hyaluronic acid (ha) and chitosan hydrochloride (hcs), to overcome multidrug resistance (MDr) in breast tumors. The nanoparticles are designed to co-load two therapeutic agents, mitoxantrone (MTO) and verapamil (VrP), to enhance their efficacy against MDr show in Fig. 2 (Jessica *et al*., 2021).

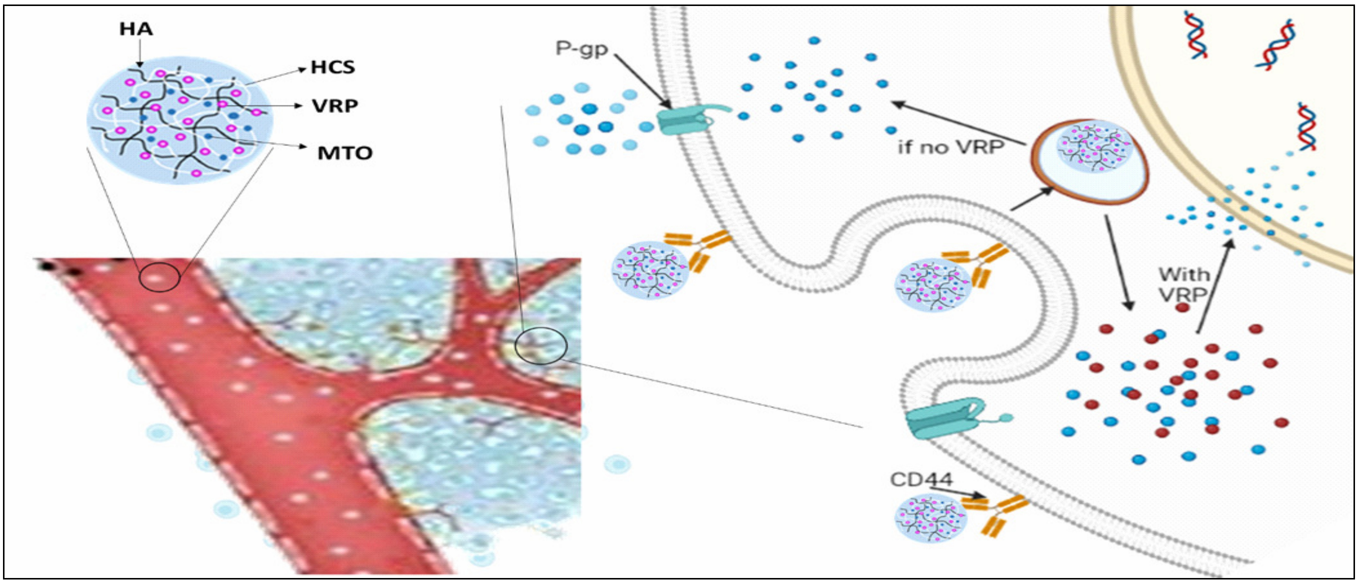

Fig. 2 : The schematic illustration depicts the formation of nanoparticles using two polysaccharide-based materials.

Formation of Nanoparticles

The illustration shows the interaction between negatively charged hyaluronic acid (ha) and positively charged chitosan hydrochloride (hcs), which leads to the formation of stable nanoparticles (Shih-Jiuan Chiu, Su-Yuan Wang *et al.,* 2014). The electrostatic attraction between the two polymers results in the encapsulation of the drug combination within the nanoparticle structure (Maya Molco *et al*., 2023).

Co-loading of MTO and VrP

Inside the formed nanoparticles, the two therapeutic agents, MTO and VrP, are co-loaded (Jessica E. Bickel, Anna Ellis *et al*., 2021). This co-loading strategy aims to sensitize the tumours cells to MTO by inhibiting the efflux pump activity mediated by P-glycoprotein, which is responsible for multidrug resistance (Hossein Adelnia, Idriss Blakey *et al*., 2023). Verapamil, acting as a P-glycoprotein inhibitor, can overcome the resistance to MTO, making the treatment more effective against drug-resistant breast tumours (Wen-Hao Fan, Jie Zhou *et al*., 2023).

Targeting with Hyaluronic Acid

Hyaluronic acid (ha) on the surface of the nanoparticles serves a dual purpose. Firstly, it helps to improve the stability of the nanoparticles (Olivier Gazil *et al.*, 2022). Secondly, ha has an affinity for CD44 receptors, which are overexpressed in many breast tumours cells (Sascha Schmitt, Lutz Nuhn *et al.*, 2022). This active targeting allows the nanoparticles to accumulate preferentially in the tumours microenvironment, increasing drug delivery to the cancer cells and reducing off-target effects (Tahira Pirzada, Mariam Sohail *et al.*, 2022).

In conclusion, the schematic illustration showcases the design of polysaccharide-based nanoparticles co-loading MTO and VrP (Jessica *et al.*, 2021). Through this innovative approach, the nanoparticles can effectively overcome multidrug resistance (MDr) in breast tumours, potentially improving the therapeutic outcome for patients with drug-resistant breast cancer (Simeon Göttert, Irina Salomatov *et al.*, 2022).

Cellulose Nanoparticles

Cellulose is a polysaccharide that is found in various natural sources such as cotton, wood, and plant fibres (Marianna Mamusa, Claudio Resta *et al.*, 2021). Cellulose nanoparticles have been studied for drug delivery due to their biocompatibility, biodegradability, and low toxicity (Marianna Mamusa, Rosangela Mastrangelo *et al.*, 2021). They can be used for targeted drug delivery by modifying their surface with ligands that bind to specific receptors (Simeon Göttert, Irina Salomatov *et al.*, 2022). Cellulose nanoparticles can also be used for sustained drug release by controlling their size and surface charges (Alexander Plucinski, ZanLyu *et al.*, 2021).

Polysaccharide-based nanoparticles are a promising class of biomaterials that have attracted significant attention in recent years for various biomedical applications (Jessica *et al.*, 2021). The development of these nanoparticles has opened up new avenues for drug delivery, imaging, and tissue engineering, as they offer several advantages such as biocompatibility, biodegradability, and the ability to be easily functionalized with targeting moieties (Henrique *et al.*, 2021). While many types of polysaccharide-based nanoparticles have been developed and characterized, further research is needed to optimize their properties and investigate their potential for clinical translation (Xibo Yan *et al.*, 2021).

Properties of polysaccharides based Nanoparticles

Properties related to the polysaccharides based nano particles show in Fig. 3. (Martin *et al.*, 2021)

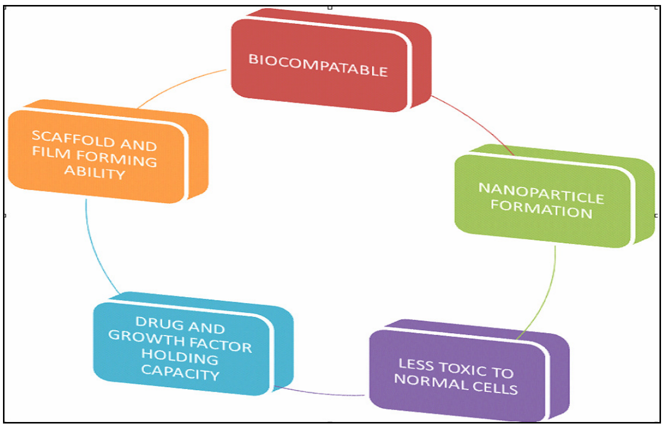

Fig. 3 : Properties of polysaccharides based Nanoparticles

Biocompatibility

One of the key advantages of polysaccharide-based nanoparticles is their biocompatibility (BoštjanVihar, Jan Rožanc *et al.*, 2021). These nanoparticles are derived from natural polysaccharides such as chitosan, alginate, cellulose, and starch, which are biocompatible and biodegradable (Hua Zhang, Peiwen Liu, *et al.*, 2019). This property makes them ideal for drug delivery applications as they do not elicit any significant immune response or toxicity (AsmaaElzayat, Inés Adam-Cervera *et al.*, 2021).

Targeting ability

Polysaccharide-based nanoparticles can be functionalized with various targeting ligands such as antibodies, peptides, and aptamers (Cynthia Cordt, Tobias Meckel *et al.*, 2020). These ligands can specifically bind to the receptors expressed on the surface of target cells, leading to enhanced cellular uptake and improved therapeutic efficacy (Jiaxiu Wang, Kai Zhang, 2018).

Controlled release

Polysaccharide-based nanoparticles can be designed to release their payload in a controlled manner (Debasish Saha, Sugam *et al.*, 2020). This property is attributed to the ability of these nanoparticles to form stable and compact structures that can encapsulate and protect the payload from degradation (Nursyahidatul Azwa Awang, Azura Amid *et al.*, 2020). The release of the payload can be triggered by various stimuli such as pH, temperature, and enzymes (Miaosi Li, Lei Bao *et al.*, 2018).

Stability

Polysaccharide-based nanoparticles are stable in various biological environments, such as blood and other body fluids (Martin Gericke, Peter Schulze *et al.*, 2020). They are also stable during the formulation and storage process, which is essential for their use in drug delivery applications (Miaosi Li, Lei Bao *et al.*, 2018).

Biodegradability

Polysaccharide-based nanoparticles are biodegradable, which means that they can be broken down into smaller components by biological processes (DebasishSaha, Sugam Kumar *et al.*, 2020). This property is essential for the clearance of the nanoparticles from the body, which minimizes their accumulation and potential toxicity (Hua Zhang, Peiwen Liu *et al.*, 2019).

Immunomodulatory properties: Polysaccharide-based nanoparticles have been shown to have immunomodulatory properties (Chao Qiu, Yao Hu, Zhengyu Jin *et al.*, 2019). For example, chitosan nanoparticles have been shown to stimulate the immune system by promoting the production of cytokines and activating macrophages (Yuliang Wang, Binglin Zeng *et al.*, 2019). This property makes them attractive for vaccine delivery applications (Ruyuan Song, Chuan Peng Zhang *et al.*, 2019).

High loading capacity

Polysaccharide-based nanoparticles have a high loading capacity for various types of payloads such as drugs, proteins, and nucleic acids (Peter Schulze, Martin Gericke *et al.,* 2019). This property is attributed to their ability to form stable and compact structures that can encapsulate a large amount of payload(Jabran Saroia, Wang Yanen *et al.*, 2018).

Tunable size and shape

Polysaccharide-based nanoparticles can be synthesized in various sizes and shapes, which can be tuned for specific applications (Miaosi Li, Lei Bao *et al*., 2018). For example, spherical nanoparticles are ideal for cellular uptake, whereas rod-shaped nanoparticles can be used for drug delivery to the central nervous system (Shuo Huang, Xin Wei, Mingfeng Wang, 2018).

Low cost

Polysaccharide-based nanoparticles can be synthesized from natural polysaccharides such as chitosan and alginate, which are readily available and inexpensive (AsmaaElzayat, Inés Adam-Cervera *et al*., 2021). This property makes them attractive for large-scale production and commercialization (Jiaxiu Wang, Kai Zhang, 2018).

Environmental friendliness

Polysaccharide-based nanoparticles are environmentally friendly as they are derived from natural polysaccharides that are renewable and biodegradable (Martin Gericke, Lars Gabriel *et al*., 2018). This property makes them attractive for sustainable and green technologies (Shuo Huang, Xin Wei, Mingfeng Wang, 2018).

In conclusion, polysaccharide-based nanoparticles have unique properties that make them attractive for various biomedical applications (Rafael Muñoz-Espí *et al*., 2018). These nanoparticles are biocompatible, have targeting ability, can release their payload in a controlled manner, are stable, biodegradable, have immunomodulatory properties, have a high loading capacity, tuneable size and shape, are low cost, and environmentally friendly (Jiaxiu Wang, Kai Zhang, 2018). These properties make them ideal for drug delivery, vaccine delivery, imaging, and other biomedical applications (AsmaaElzayat, Inés Adam-Cervera *et al*., 2021).

Pathological effects

Polysaccharide-based nanoparticles (PNPs) are a type of Nano carrier that have gained significant interest in drug delivery applications due to their biocompatibility, biodegradability, and low toxicity. However, like any other Nano carrier system, PNPs can induce certain pathological effects that must be thoroughly investigated (Rafael Muñoz-Espí, Olaia Álvarez-Bermúdez, 2018).

The potential pathological effects of PNPs can be broadly categorized into two types: acute and chronic (Martin Gericke, Lars Gabriel *et al*., 2018). Acute effects al. 2018 refer to the immediate physiological response of the body to PNPs upon exposure (Sheva Naahidi, Mousa Jafari *et al*., 2017). These can include inflammation, oxidative stress, and immune system activation (Martin Gericke, Lars Gabriel *et al*., 2018). Chronic effects refer to the long-term pathological effects of PNPs that develop over time (Debasish Saha, Sugam Kumar *et al*., 2020). These can include accumulation of PNPs in vital organs, Geno toxicity, and carcinogenicity (Aisha Roshan Mohamed Wali *et al*., 2017).

The specific pathological effects of PNPs depend on several factors such as their size, surface charge, surface chemistry, and mode of administration (Debasish Saha, Sugam Kumar *et al*., 2020). For instance, positively charged

PNPs tend to induce higher levels of inflammation and oxidative stress compared to negatively charged or neutral PNPs (Aisha Roshan Mohamed Wali *et al*., 2017). Similarly, larger PNPs tend to accumulate in the liver and spleen, while smaller PNPs tend to accumulate in the kidneys (Rohollah Sadeghi, Laleh Mehryar *et al*., 2017).

To mitigate the potential pathological effects of PNPs, researchers are exploring various strategies such as surface modification, co-administration of antioxidants, and use of biodegradable polymers (Aisha Roshan Mohamed Wali *et al*., 2017). These strategies aim to improve the biocompatibility and safety profile of PNPs for drug delivery applications (Debasish Saha, Sugam Kumar *et al*., 2017).

Immunological Pathology

Polysaccharide-based nanoparticles can interact with the immune system in various ways, depending on their physicochemical properties (Nursyahid atul Azwa Awang *et al*., 2020). For example, nanoparticles that are too large may be recognized as foreign bodies and trigger an immune response (Haitao Yu, Shantanu Maheshwari *et al*., 2017). This can lead to the activation of immune cells such as macrophages and dendritic cells, which can release pro-inflammatory cytokines and cause tissue damage (Sheva Naahidi, Mousa Jafari *et al*., 2017). Similarly, nanoparticles that have a positive surface charge may interact with negatively charged cell membranes and trigger an immune response (Paolo Zucca, Roberto Fernandez- Lafuente *et al*., 2016). This can also lead to the release of pro-inflammatory cytokines and tissue damage (Marianna Mamusa, Rosangela Mastrangelo *et al*., 2021).

Toxicological Pathology

Polysaccharide-based nanoparticles can also have toxic effects on biological systems(Alexander Plucinski, ZanLyu *et al*., 2021). This can occur due to the release of toxic components during the synthesis or degradation of the nanoparticles (Carlos Gregorio Barreras-Urbina *et al*., 2016). For example, chitosan nanoparticles can release acetic acid during degradation, which can cause tissue damage (Asmaa Elzayat, Inés Adam-Cervera *et al*., 2021). Similarly, alginate nanoparticles can release calcium ions during degradation, which can cause calcium deposition and tissue damage (Peter Schulze, Martin Gericke *et al*., 2016). Toxicological pathology can also occur due to the accumulation of nanoparticles in specific organs or tissues, leading to toxicity (Conxita Solans, Daniel Morales, Maria Homs, 2016).

Graphical abstract of polysaccharides based Nano particles for Theranostic Nanomedicines shown in Fig. 4. (ConxitaSolans, Daniel Morales, Maria Homs, 2016).

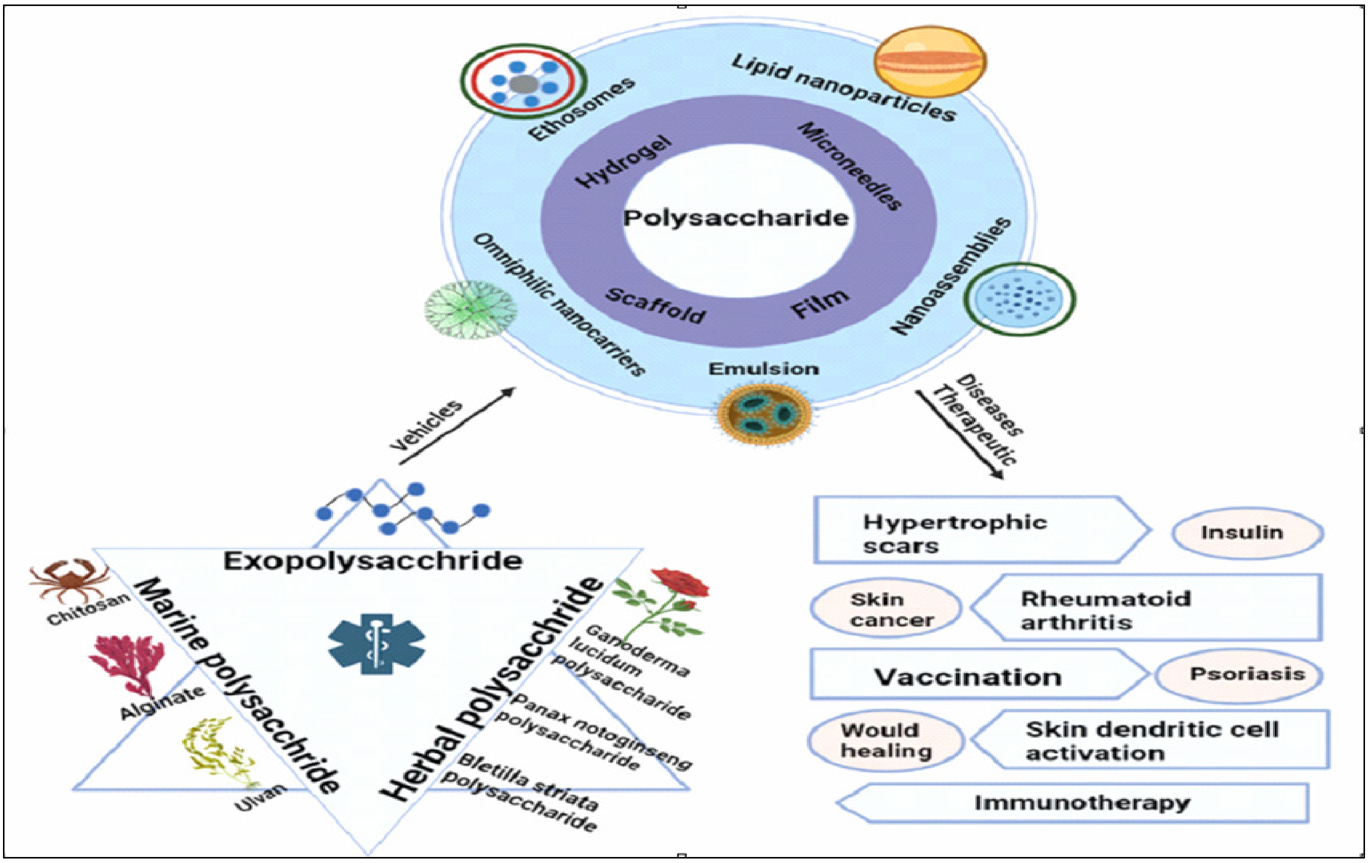

Fig. 4: Graphical aspects of Theranostic nano Medicines

Here are some key aspects of using polysaccharides-based nanoparticles for theranostic nanomedicines: (Susete N. Fernandes, Luis E. Aguirre *et al*., 2016)

Biocompatibility

Polysaccharides, such as chitosan, hyaluronic acid, dextran, and cellulose, are derived from natural sources and are generally well-tolerated by the human body (Maya Molco, Amir Keilin *et al*., 2023). This biocompatibility minimizes the risk of adverse reactions, making them suitable for biomedical applications (Chao Qiu, Yao Hu, ZhengyuJin *et al*., 2019).

Biodegradability

Polysaccharides are typically enzymatically degraded in the body, leading to the formation of non-toxic byproducts (Rohollah Sadeghi, Laleh Mehryar *et al*., 2016). This characteristic ensures that the nanoparticles can be safely metabolized and eliminated from the body after fulfilling their therapeutic and diagnostic functions (Farouk Ayadi, Ilker S. Bayer *et al*., 2016).

Encapsulation of Therapeutic Agents: Polysaccharides-based nanoparticles can encapsulate a wide range of therapeutic agents, such as chemotherapeutic drugs, siRNA, proteins, and even imaging contrast agents (Yonggui Wang, Thomas Heinze *et al*., 2016).The encapsulation protects the cargo from degradation and clearance in the body, allowing for targeted delivery and controlled release at the disease site (Detlef Lohse, Xuehua Zhang, 2015).

Targeting Capabilities

The surface of polysaccharides-based nanoparticles can be easily modified with targeting ligands, such as antibodies or peptides, that specifically recognize receptors over expressed on diseased cells (Qifeng Wang, Sadaki Samitsu *et al*., 2015). This targeting ability enhances the nanoparticle's accumulation at the intended site, reducing off-target effects and improving therapeutic efficacy (Kai Zhang, Andreas, *et al*., 2015).

Imaging Modalities

Polysaccharides themselves can serve as contrast agents for certain imaging modalities due to their inherent properties, such as optical or magnetic resonance imaging (AsmaaElzayat, Inés Adam-Cervera *et al*., 2021). Additionally, the surface of the nanoparticles can be functionalized with imaging agents to enable real-time monitoring of drug delivery and treatment response (Sumanta Kumar Ghosh, Farooque Abdullah *et al*., 2015).

Stimuli-Responsive Behaviour

Some polysaccharides can respond to specific environmental stimuli, such as pH, temperature, or enzymatic activity (Qifeng Wang, SadakiSamitsu *et al*., 2015). This property can be harnessed to design smart nanoparticles that release their therapeutic payload in response to specific cues present at the disease site (Pietro Locatelli, Steve Woutters *et al*., 2015).

Reduced Immunogenicity

Polysaccharides generally exhibit lower immunogenicity compared to synthetic polymers, reducing the risk of immune responses and potential complications associated with repeated administration (AsmaaElzayat, Inés Adam-Cervera *et al*., 2021).

Pharmacological Pathology

Polysaccharide-based nanoparticles can also have pharmacological effects on biological systems (Paolo Zucca, Roberto Fernandez-Lafuente *et al*., 2016). This can occur due to the drug payload carried by the nanoparticles or due to the interaction of the nanoparticles with biological targets (Martin Gericke, Lars Gabriel *et al*., 2018). For example, chitosan nanoparticles can enhance the bioavailability and efficacy of certain drugs by protecting them from degradation and increasing their absorption (Debasish Saha, Fabienne Testard *et al*., 2015). Similarly, alginate nanoparticles can be used for targeted drug delivery by conjugating them with ligands that bind to specific receptors (Frederik R. Wurm, Clemens K. Weiss, 2014). However, pharmacological pathology can also occur if the nanoparticles interact with unintended targets, leading to off-target effects and toxicity (Andreas Geissler, Markus Biesalski *et al*., 2014).

Genotoxic Pathology

Polysaccharide-based nanoparticles can also have genotoxic effects on biological systems (Kerstin Malzahn, William D. Jamieson *et al*., 2014). This can occur due to the interaction of the nanoparticles with DNA or other genetic material, leading to mutations or other genetic changes (DebasishSaha, Fabienne Testard *et al*., 2015). For example, cellulose nanoparticles can induce DNA damage and chromosomal aberrations in human cells (Chenglong Xu, Shuhua Peng *et al*., 2014). Similarly, chitosan nanoparticles can cause DNA damage in fish embryos (Y. Liu, Y. C. Lu, G. S. Luo, 2014). Geno toxic pathology can also occur due to the release of toxic components during the synthesis or degradation of the nanoparticles (Santana, C.P., Mansur, A.A.P *et al*., 2020).

Haematological Pathology

Polysaccharide-based nanoparticles can interact with the blood and the circulatory system, leading to haematological pathology (Martin Gericke, Lars Gabriel *et al*., 2018). For example, nanoparticles that are too large may block blood vessels and cause thrombosis, leading to tissue damage and organ failure (Servais *et al*. 2018). Similarly, nanoparticles that have a positive surface charge may interact with red blood cells and cause haemolysis, leading to anaemia and other blood disorders (Chenglong Xu, Shuhua Peng *et al*., 2014). Haematological pathology can also occur due to the accumulation of nanoparticles in the liver or spleen, leading to changes in blood composition and function (Silva *et al*., 2020).

Polysaccharide-based nanoparticles have great potential for drug delivery and other biomedical applications (Uccello-Barretta *et al*., 2013). However, it is important to understand the potential pathological effects they may have on biological systems (Wei *et al*., 2020). Immunological, toxicological, pharmacological, genotoxic, and haematological pathology are some of the types of pathology that can occur with polysaccharide-based nanoparticles (Zhang *et al*., 2016). By understanding these potential effects, researchers can design safer and more effective nanoparticles for biomedical applications (Zhang and Feng, 2013).

TREATMENT

Polysaccharide-based nanoparticles have attracted considerable attention in the field of drug delivery due to their biocompatibility, biodegradability, and versatility (Lucke, *et al*., 2005). These nanoparticles can be used to encapsulate drugs and target specific tissues, thereby improving the efficacy and safety of various therapeutics (Antman-Passig and Shefi, 2016). In this article, we will discuss the different types of treatment that can be achieved using polysaccharide-based nanoparticles and the advantages they offer (Xu *et al*., 2011). Green synthesis of nano particles given in table 2 and modifications shown in Fig. 5.

Table 2 : Green synthesis of polysaccharides Based nanoparticles

Green synthesis of nanopolysaccharides		
Top down approach (size reduction)		Bottom uo approach (self- assembly)
Physical treatment	Chemical treatment	Metallic precursor
Mechanical milling; Thermal ablation; sputtering	Chemical etching	Nucleation and nanosaccharides formation

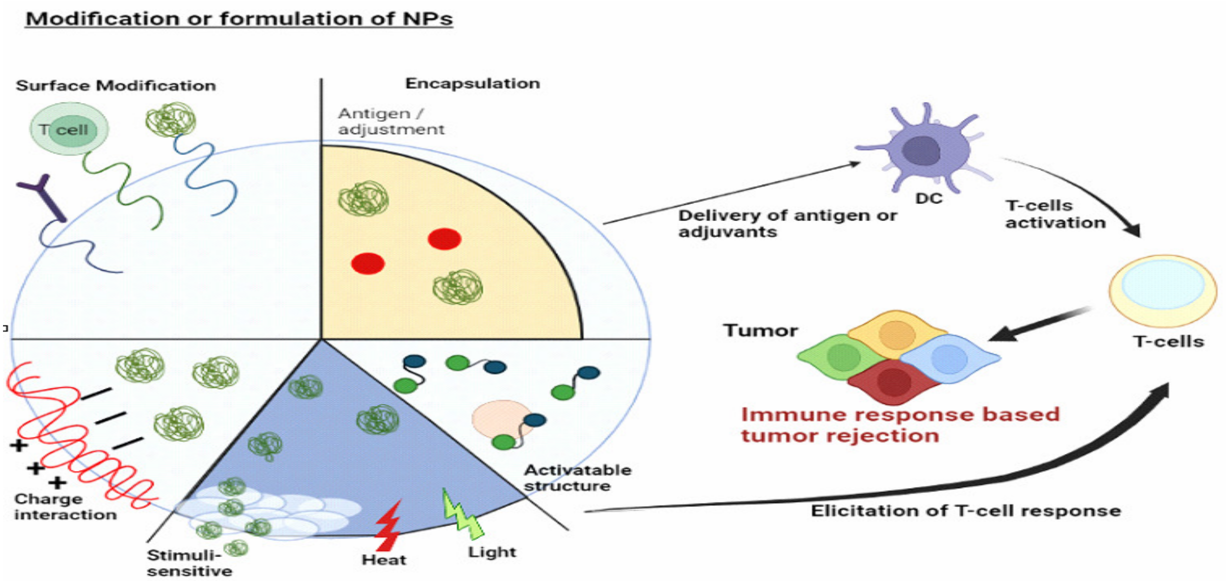

Fig. 5 : Modifications and formulations of NPs

Surface functionalization

Nanoparticles' surfaces can be modified by attaching specific molecules, polymers, or biomolecules to improve stability, solubility, and targeting capabilities (Hossain *et al.*, 2019). This is particularly important in drug delivery, where functionalizing nanoparticles can enhance their ability to deliver drugs to specific cells or tissues (Qiu *et al.*, 2018).

Core-shell structures

Core-shell nanoparticles have a core made of one material and a shell made of another (Mollazadeh *et al.*, 2021). This design provides additional functionality and control over properties (Li *et al.*, 2017). For instance, a magnetic core could be surrounded by a polymer shell to improve biocompatibility for biomedical applications (Datta *et al.*, 2017).

Doping

Introducing impurities (dopants) into the nanoparticle's structure can alter its electronic or optical properties (Gunawan *et al.*, 2015). This is widely used in semiconductor nanoparticles (quantum dots) to tune their emission wavelength or enhance their electrical conductivity (Shi *et al.*, 2020).

Nanoemulsions

Nanoemulsions consist of nanoscale droplets of one liquid dispersed in another immiscible liquid (Hossain *et al.*, 2019). These systems have applications in drug delivery, food, and cosmetics, as they improve solubility and bioavailability (Huang *et al.*, 2020).

Coating with metals

Coating nanoparticles with metals, such as gold or silver, can enhance their optical properties, making them useful for imaging, diagnostics, and photothermal therapy (Lu *et al.*, 2020).

Mesoporous nanoparticles

These nanoparticles have a porous structure with high surface area and can be used as carriers for drug molecules or for catalytic applications (Bhattacharya *et al.*, 2016).

Hybrid nanoparticles

Combining different types of nanoparticles or nanoparticles with other materials (e.g., carbon nanotubes) can lead to new functionalities and applications (Yu *et al.*, 2018).

pH- sensitive nanoparticles

Some nanoparticles can be engineered to release their payloads in response to changes in pH levels, which is valuable for targeted drug delivery (Hossain *et al.*, 2019).

Magnetic nanoparticles

Adding magnetic properties to nanoparticles enables their manipulation and guidance using external magnetic fields, making them suitable for targeted drug delivery and imaging (Chen and Jianzhong, 2013).

Bio-inspired nanoparticles

Designing nanoparticles inspired by biological systems can lead to innovative solutions, such as biomimetic drug delivery carriers or bioactive coatings (Hossain *et al.*, 2019).

Anti-inflammatory Treatment

The treatment of inflammation using polysaccharide-based nanoparticles involves the encapsulation of anti-inflammatory agents within nano-sized polysaccharide carriers (Młynek *et al.*, 2023). This approach offers several advantages over conventional methods of drug delivery, as mentioned earlier (Lee *et al.*, 2007).

Here's a more detailed explanation of how this treatment works:

Drug Encapsulation

First, the anti-inflammatory drug or agent is encapsulated within the nano-sized polysaccharide particles (Choi *et al.*, 2010). Polysaccharides like chitosan, alginate, hyaluronic acid, and others are commonly used for this purpose due to their biocompatibility and ability to form stable nanoparticles (Yang *et al.*, 2015).

Targeted Delivery

The nanoparticles can be designed to target specific inflamed tissues or cells by functionalizing their surface with ligands or antibodies that bind to receptors expressed in the inflamed regions (Zhao *et al.*, 2015). This targeting ensures that the drug is delivered directly to the site of inflammation, reducing the exposure of healthy tissues to the drug and minimizing potential side effects (Meng *et al.*, 2016).

Sustained Release

Polysaccharide-based nanoparticles can be engineered to release the encapsulated drug slowly and steadily (Chi *et al.*, 2017). This sustained release allows for a prolonged therapeutic effect, reducing the frequency of drug administration and maintaining a constant drug concentration at the target site (Xu, *et al.*, 2011).

Some polysaccharides themselves possess anti-inflammatory and immunomodulatory properties, which can further enhance the therapeutic effect (Kratz and Warnecke, 2012). For example, chitosan has been reported to reduce inflammation and promote tissue healing (Ju *et al.*, 2016).

Bioavailability Improvement

Polysaccharide-based nanoparticles can improve the solubility and stability of poorly water-soluble anti-inflammatory drugs, thereby increasing their bioavailability and overall effectiveness.

Reduction of Systemic Toxicity

By delivering the drug directly to the inflamed tissue, the systemic exposure of the drug is reduced, which can minimize potential toxic effects on other organs and tissues (Tang *et al.*, 2014).

Combination Therapy

Polysaccharide-based nanoparticles can carry multiple therapeutic agents simultaneously, enabling combination therapy with different anti-inflammatory drugs or even other medications targeting related conditions (Chen *et al.*, 2015).

It's Important to note that the success of polysaccharide-based nanoparticles as an anti-inflammatory treatment depends on several factors, including the choice of polysaccharide, the drug being encapsulated, nanoparticle size, surface modification for targeting, and the specific characteristics of the inflammation being treated

(Čalija *et al*., 2014).

As with any new medical treatment, further research, preclinical studies, and eventually clinical trials are necessary to validate the efficacy, safety, and potential benefits of using polysaccharide-based nanoparticles for anti-inflammatory therapy (Liu *et al*., 1999). While the technology shows promise, it is still an area of active research and development (He *et al*., 2011).

Cancer Treatment

Cancer therapy using polysaccharide-based nanoparticles is an emerging area of research in the field of nanomedicine (Chen, 1994). Polysaccharides are long chains of sugar molecules that can be derived from various natural sources, such as plants, fungi, and bacteria (Chen *et al*., 2015). They possess unique properties that make them attractive for nanoparticle-based drug delivery systems (Tsuchida *et al*., 1976).

Nanoparticles are tiny particles with sizes typically ranging from 1 to 100 nanometers (Chen *et al*., 2015). By encapsulating drugs within these nanoparticles, it is possible to improve the drug's stability, solubility, and bioavailability, as well as target its delivery to specific tissues or cells, including cancer cells (Chen *et al*., 2015).

Here are some ways In which polysaccharide-based nanoparticles are being used in cancer therapy:

Drug delivery

Polysaccharide nanoparticles can act as carriers for chemotherapeutic drugs (Jewell *et al*., 2006). By entrapping the drugs within the nanoparticles, they can be protected from degradation, avoid premature clearance from the body, and be delivered specifically to tumor sites through passive or active targeting mechanisms (Chen *et al*., 2015). This targeted drug delivery reduces systemic side effects and enhances the effectiveness of the treatment (Halder *et al*., 2005).

Immunotherapy

Polysaccharides have intrinsic immunomodulatory properties (Hossain *et al*., 2019). They can stimulate the immune system, promoting the body's natural defense mechanisms against cancer cells (Karibyants and Dautzenberg, 1998). Polysaccharide-based nanoparticles can be loaded with antigens or other immune-stimulating agents to boost the body's immune response against cancer (Schatz *et al*., 2004).

Photo thermal therapy (PTT) and photodynamic therapy (PDT): Polysaccharide nanoparticles can be engineered to have photo absorbing or photosensitizing properties (Buchhammer *et al*., 2003). When exposed to light of a specific wavelength, these nanoparticles can generate heat (PTT) or reactive oxygen species (PDT) to selectively destroy cancer cells (Stavrovskaya, 2000).

Imaging

Polysaccharide nanoparticles can also be designed to carry imaging agents, such as fluorescent dyes or contrast agents for various imaging modalities like MRI, CT, or PET (Chen *et al*., 2015). This enables non-invasive monitoring of the treatment's progress and the targeted delivery of the therapeutic nanoparticles to the tumor site (Song *et al*., 2009).

Combination therapy

Polysaccharide-based nanoparticles offer the opportunity to combine multiple therapeutic agents (chemotherapeutic drugs, immunomodulatory, and more) within a single nanoparticle system (Niu *et al*., 2013). This approach can enhance the therapeutic effects and overcome drug resistance in cancer cells (Su *et al*., 2014).

Biocompatibility and biodegradability

Polysaccharides are generally biocompatible and biodegradable, which makes them suitable for use in the human body (Chen *et al*., 2015). They minimize the risk of toxicity and side effects associated with non-biodegradable nanoparticles (Wong *et al*., 2004).

It's Important to note that while polysaccharide-based nanoparticles show great promise for cancer therapy, there are still challenges in terms of optimizing their properties, scalability, and ensuring their safety and efficacy for clinical use (Febvay *et al*., 2010). Research in this field is ongoing, and the development of these innovative nanomedicine approaches holds significant potential for improving cancer treatment in the future (Reszka *et al*., 1997).

Gene Therapy

Gene therapy using polysaccharide-based nanoparticles is an emerging field of research in the medical and biotechnological industries (Imai *et al*., 2004). Polysaccharides are complex carbohydrates composed of long chains of sugar molecules, and they have unique properties that make them suitable for various biomedical applications, including gene delivery (Huang *et al*., 2016).

The primary goal of gene therapy is to introduce therapeutic genetic material into the cells of a patient to treat or prevent diseases caused by genetic mutations or deficiencies (Chen *et al*., 2015). Traditional gene therapy approaches often use viral vectors to deliver the therapeutic genes into the target cells (Amin, 2013). However, using viruses can raise safety concerns, such as immunogenicity and potential adverse effects (Čalija *et al*., 2015).

Polysaccharide-based nanoparticles offer an attractive alternative as non-viral gene delivery vectors due to their biocompatibility, biodegradability, and low immunogenicity (Tsuruo *et al*., 1981). Some commonly used polysaccharides for gene delivery include chitosan, alginate, hyaluronic acid, dextran, and cyclodextrins. These polysaccharides can be chemically modified to improve their stability, encapsulation efficiency, and cellular uptake (Muller *et al*., 1995).

Here's a general outline of how gene therapy using polysaccharide-based nanoparticles works:

Nanoparticle preparation

Polysaccharides are chemically modified and assembled into nanoparticles through techniques like nanoprecipitation, emulsification, or electrostatic complexation (Tsubaki *et al*., 2014).

Gene encapsulation

The therapeutic genes (DNA or RNA) are loaded into the nanoparticles, which protect the genetic material from degradation and enhance its stability during delivery (Nikolaeva *et al*., 2000).

Targeting and cellular uptake

To improve the efficiency of gene delivery, the nanoparticles can be functionalized with targeting ligands, such as antibodies or peptides, that specifically bind to receptors on the target cells. This allows the nanoparticles to be taken up more readily by the desired cells (Eliaz and Szoka, 2001 2001).

Intracellular delivery

Once taken up by the target cells, the nanoparticles release the therapeutic genes, which can then enter the cell nucleus and exert their therapeutic effects (Yoon *et al*., 2012).

Gene expression and therapeutic outcome

The delivered genes instruct the cells to produce specific proteins that can correct a genetic defect, suppress the expression of a harmful gene, or trigger other therapeutic responses (Zauner *et al*., 2001).

Polysaccharide-based nanoparticles for gene therapy have shown promising results in preclinical studies, but challenges still exist, such as achieving high transfection efficiency and controlling gene expression levels (Nikolaeva *et al*., 2000). Ongoing research aims to improve the design of these nanoparticles and optimize their properties to make them viable for clinical applications in the future (Chen *et al*., 2015). As of my last update in September 2021, some gene therapies using nanoparticles had advanced to clinical trials, but it is essential to consult up-to-date sources to see the latest developments in this rapidly evolving field (Tosi *et al*., 2008).

Wound Healing Treatment

Wound healing is a complex process that involves various cellular and molecular events. Polysaccharides, which are long chains of carbohydrates, have shown great potential in wound healing due to their biocompatibility, biodegradability, and ability to mimic the extracellular matrix, which is essential for tissue regeneration (Ulbrich *et al*., 2011). When polysaccharides are used in the form of nanoparticles, they can enhance wound healing even further by providing controlled release of therapeutic agents, improved stability, and targeted delivery (Schork *et al*., 2005).

Here's an overview of how wound healing treatment using polysaccharide-based nanoparticles works:

Polysaccharide Selection

Researchers choose specific polysaccharides based on their properties and potential therapeutic effects (Senear and Teller, 1981). Commonly used polysaccharides for wound healing include chitosan, hyaluronic acid, alginate, and cellulose derivatives (Tiegs *et al*., 1992).

Nanoparticle Formation

Polysaccharides are processed to form nanoparticles (Mo *et al*., 2007). Techniques such as nanoprecipitation, emulsification, or ionic gelation can be used to create nanoparticles with the desired size, shape, and surface properties (Nikolaeva *et al*., 2000).

Incorporation of Therapeutic Agents

Polysaccharide nanoparticles can be loaded with various therapeutic agents, such as growth factors, antimicrobial agents, or anti-inflammatory drugs (Leroux *et al*., 1996). These agents aid in promoting wound healing, preventing infection, and reducing inflammation (Medeiros *et al*., 2010).

Application to Wound Site

The polysaccharide-based nanoparticles are applied directly to the wound site (Chen *et al*., 2015). They can be formulated as a gel, spray, or dressing, depending on the wound type and severity (Hattori *et al*., 2009).

Polysaccharide-based nanoparticles facilitate wound healing through several mechanisms:

Moist Wound Healing Environment

They help maintain a moist environment at the wound site, which is crucial for cell migration and tissue regeneration (Chen and Davis, 2002).

Cell Adhesion and Migration

Polysaccharides mimic the extracellular matrix, promoting cell adhesion and migration, which are essential for tissue repair (Cetin *et al*., 2010).

Controlled Release of Therapeutic Agents

The nanoparticles release therapeutic agents in a controlled manner, providing a sustained effect at the wound site (Zinn *et al*., 2001).

Anti-inflammatory and Antimicrobial Effects: Some polysaccharides possess inherent anti-inflammatory and antimicrobial properties, reducing the risk of infection and inflammation (Rello *et al*., 2006).

Enhanced Healing Process: By providing a conducive environment and targeted delivery of therapeutic agents, polysaccharide-based nanoparticles can accelerate the wound healing process, minimize scar formation, and improve tissue regeneration (Khan, 2018).

It's important to note that while research in this field shows promising results, wound healing is a complex process that can vary from person to person (Raeisi and Raeisi, 2023). The use of polysaccharide-based nanoparticles for wound healing is still an area of ongoing research, and further studies are needed to optimize formulations, understand long-term effects, and ensure the safety and efficacy of these treatments (Chen *et al*., 2015). Always consult with a healthcare professional for proper wound care and treatment (Maciel *et al*., 2016).

Vaccines:

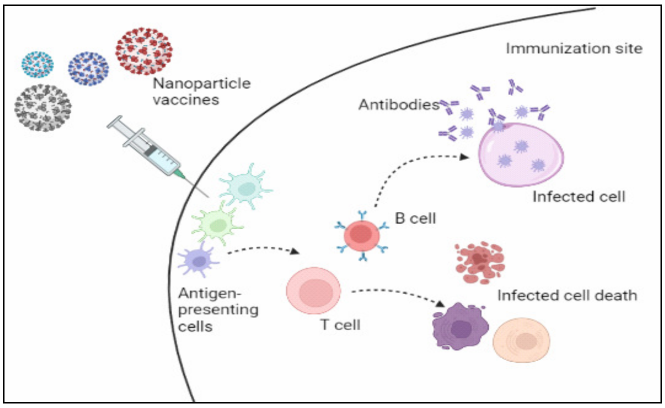

Fig. 6 : Formulated vaccines from nanoparticles

Polysaccharide-based nanoparticles can also be used to develop vaccines by delivering antigens and adjuvants to the immune system (Nikolaeva *et al*., 2000). For example, chitosan nanoparticles have been used to deliver ovalbumin, a model antigen, and CpG oligonucleotides, an adjuvant, to the immune system to induce an immune response as shown in figure 6 (Xibo Yan, Julien Bernard, François Ganachaud, 2021). Similarly, alginate nanoparticles have been used to deliver influenza antigens and induce a protective immune response in mice (Beaumont *et al*., 2021).

Polysaccharide-based nanoparticles offer numerous advantages for drug delivery and other biomedical applications (Onofre-Cordeiro *et al*., 2018). They are biocompatible, biodegradable, and can be easily functionalized to target specific cells and tissues (Manivasagan and Oh, 2016). Cancer treatment, anti-inflammatory treatment, gene therapy, wound healing, and vaccines are some of the types of treatment that can be achieved using polysaccharide-based nanoparticles (Xibo Yan, Julien Bernard, François Ganachaud, 2021). By effective therapies for various diseases.

Microbial Polysaccharide-Based Nano formulations for Nutraceutical Delivery

Microbial polysaccharides have gained considerable interest in recent years due to their potential as materials for Nano formulations in various applications, including nutraceutical delivery (Xibo *et al*., 2021). Nano formulations are submicron-sized structures that can improve the stability, bioavailability, and targeted delivery of bioactive compounds, such as nutraceuticals, which are natural bioactive compounds with potential health benefits (Sun *et al*., 2021).

Microbial polysaccharides are polysaccharides produced by microorganisms such as bacteria, fungi, or algae (Kidgell *et al*., 2019). Some examples of microbial polysaccharides include bacterial cellulose, dextran, alginate, pullulan, and chitosan, among others (Xibo *et al*., 2021). These polysaccharides possess unique properties, such as biocompatibility, biodegradability, and ease of modification, making them suitable candidates for various biomedical and pharmaceutical applications, including nutraceutical delivery (McKim *et al*., 2019).

The utilization of microbial polysaccharides in nutraceutical Nano formulations offers several advantages:

Biocompatibility and Biodegradability

Microbial polysaccharides are typically non-toxic and biocompatible, meaning they can be safely used in the human body without adverse effects (Frediansyah, 2021). Moreover, they are biodegradable, which ensures the elimination of the carrier material after its purpose is served, reducing potential environmental concerns (Kamat *et al*., 2010).

Encapsulation and Protection

Nano formulations based on microbial polysaccharides can encapsulate nutraceutical compounds, providing protection against degradation caused by environmental factors such as heat, light, and moisture (Choi *et al*., 2012). This protection helps to maintain the stability and bioactivity of the nutraceuticals during storage and transportation (AsmaaElzayat *et al*., 2021).

Enhanced Bioavailability

The small particle size of Nano formulations allows for improved bioavailability of nutraceutical compounds (Podgórna *et al*., 2017). They can overcome biological barriers, such as the gastrointestinal tract's mucus layer, leading to enhanced absorption and higher bioactivity (Wong and Choi, 2015).

Targeted Delivery

Microbial polysaccharides can be modified to achieve targeted delivery of nutraceuticals to specific tissues or cells (Sethi *et al*., 2014). Functionalization of the Nano formulations with ligands that recognize specific receptors on the target cells can enhance the accumulation of nutraceuticals at the desired site of action (Pelaz *et al*., 2015).

Sustained Release

Nano formulations can be designed to release nutraceuticals in a controlled and sustained manner, which is particularly beneficial for long-term therapeutic effects (Jain and Jain, 2015).

Combination Therapy

Microbial polysaccharide-based Nano formulations can incorporate multiple nutraceuticals or even conventional drugs, enabling combination therapies for synergistic effects (Yoon *et al*., 2012).

However, there are still some challenges associated with using microbial polysaccharides for nutraceutical delivery (Anirudhan and Nair, 2018). These include issues related to scalability, reproducibility, and regulatory approval (Aldawsari and Hosny, 2018). Additionally, the choice of the appropriate polysaccharide and formulation method depends on the specific nutraceutical compound and its desired delivery requirements (D'Mello *et al.,* 2017).

Conclusion

As per the healthcare costs rise, people focusing on the healthier living, preventive care, and for the secondary sources of the medications. There is a global revolution in the nutraceuticals due to the adverse effects or can say the reactions of the drugs and there toxicity risks. Nutraceutical are the usage that can enhance the health, longevity, and the quality of the life. However, these nutraceuticals required Nano encapsulations to improve their bioactivity and then stabilize them for the targeted delivery system. In food and biomedical sciences, polysaccharides have been extensively used for the decades, and providing such significant benefits such as their biocompatibility, their nontoxicity, their consumer friendliness, their cost-effectiveness, and their ability to interact more efficiently through other biomaterials. In the light of the increasing interest in the polysaccharide-based nanomaterials has been from the last couple of years, it has been clear that these materials can be used in the various industries for the incorporation in the food products and for the nutraceuticals as a stabilizer and as a delivery agent. Different types of the microbial polysaccharides can be used in encapsulation and in the nutraceutical applications, allowing the formulators for tailor properties and for the prepared delivery systems for some specific objectives. It is also being possible to chemically modify the polysaccharides owing in the presence of the different functional groups, which can be enhance their delivery and the encapsulation performance. Composite nanomaterials with the improved properties that can be created with the help of combining the polysaccharides with other edible substances like polyphenols, proteins, or phospholipids. The combination of the functional groups that can induce multistimuli responses for controlling the release required for further consideration. Graphically validation shown in fig 7.

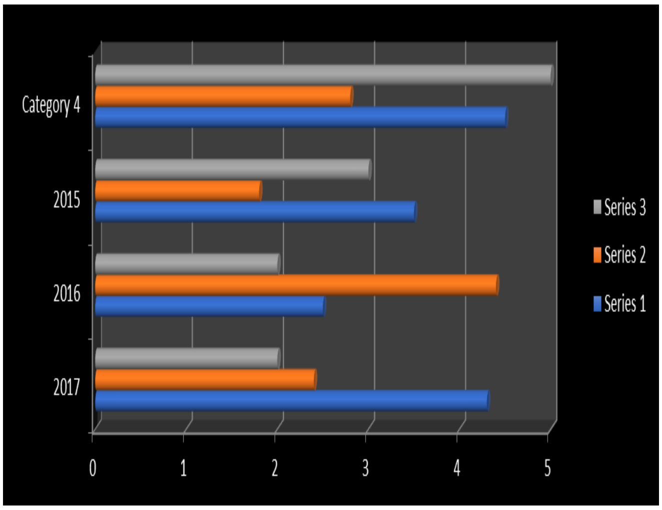

Fig. 7 : Representing the Scopus index article

The series in the graph representing the latest research demands on the basis of yearly formulation changes. The series representing following indexes of :

Series 1 polysaccharides nanoparticles

Series 2 polysaccharides based Ag(silver) nanoparticles

Series 3 represent the polysaccharide based magnetic nanoparticles

Future outlook

In addition to the delivering there are several bioactive substances in a single delivery system, the polysaccharide-based and the Nano formulations can be helpful in personalizing nutrition (Asmaa *et al*., 2021). Despite this, polysaccharide-based Nano carriers still needed to be thoroughly tested under the more realistic conditions in the in vitro and in vivo clinical trials for their safety and for the efficacy (Khor and Lim, 2003). Further there are intensive research that must be done for the specific interactions of the nanomaterials using the human organs, the tissues, cells, or with the biomolecules, and their effect on human metabolism, with some application in drug delivery (Dash *et al*., 2011). By Researching into the exact mechanisms of the polysaccharide bioactivities and their future applications that requires extensive exploration of the structural activity relationship between the polysaccharides (Kumar *et al*., 2004). This review summarizes that there are several microbial polysaccharides that are utilized for Nano formulations, such as the nanogel, nanoparticle, nanofiber, and etc. (Davoodbasha *et al*., 2016). Additionally, we have a discussion on the role and importance of the nutraceuticals along with there increasing global marketing with the rising demand (58). Finally, we have the described nano formulation techniques that ate involved in the encapsulation and the delivery system of the nutraceuticals (Termsarasab *et al*., 2013). Since there are some handful reports on microbial polysaccharide nanoformulations, it paves through the way for developing a novel nanomaterials with some of the exclusive properties, thus broadening the horizon of the nutraceutical encapsulation and of the delivery applications (Han *et al*., 2010). The development of the nanoformulated delivery systems of an essential nutraceuticals over the next few years is widely anticipating to continue, with the variety of novel food products expected to using with a significant impact on the addressing malnutrition among the children in the coming time (Wu *et al*., 2016).

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