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Bilirubin Nanomedicines for the Treatment of Reactive Oxygen Species(ROS)-Mediated Disease

Mr. Siddheshwar Sandesh Vardhaman Mr. Suryavanshi Mayur Dattatray , Mr. Bhosle Rohit Raju
Shri Amolak Jain Vidya Prasarak Mandal's, College Of PharmaceuticalScience And Research Center Kada, 414202 Ashti, Beed.

ABTRACT

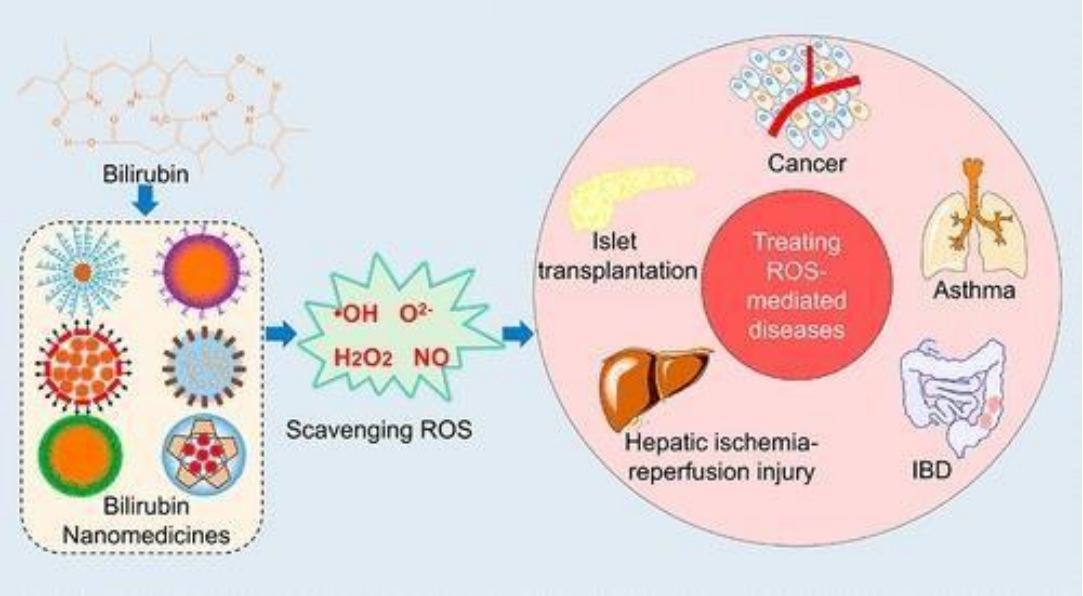
Reactive oxygen species (ROS)-mediated diseases, characterized by oxidative stress and inflammation, pose significant challenges in the field of medicine. Bilirubin, a natural antioxidant derived from heme breakdown, has shown remarkable potential in scavenging ROS and mitigating their detrimental In recent years, the development of nanomedicines has emerged as a promising approach for targeted drug delivery and enhanced therapeutic efficacy. This review explores the utilization of bilirubin nanomedicines as a novel strategy forthe treatment of ROS-mediated diseases.

Various biocompatible nanoparticles, including liposomes, polymeric nanoparticles, and lipidnanoparticles, have been employed to encapsulate bilirubin, ensuring its stability and improving its pharmacokinetics. Additionally, surface modifications of nanoparticles with ligands enable targeted delivery of bilirubin to specific cells or tissues affected by oxidative stress. Conjugation of bilirubin to nanoparticles further enhances its stability, cellular uptake,and controlled release in response to ROS or other stimuli.

Keywords: bilirubin, nanomedicines, reactive oxygen species, oxidative stress,inflammation, drug delivery, targeted therapy.

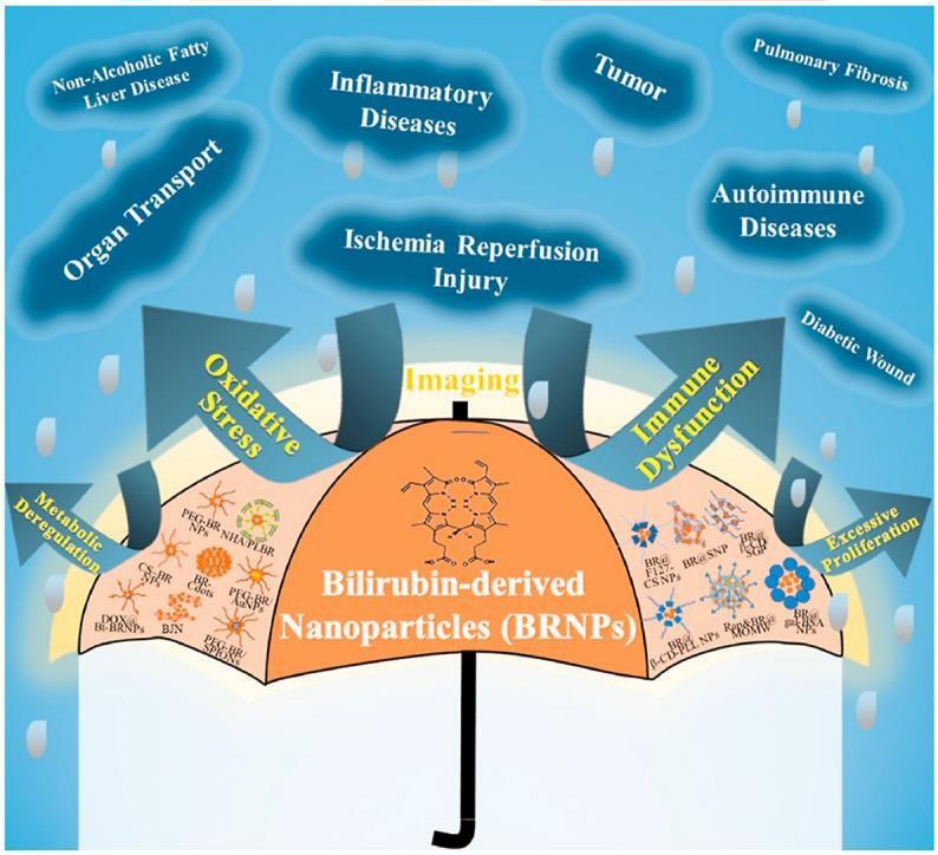
INTNRODUCTION

Reactive oxygen species (ROS) are chemically reactive species that are produced in cellular aerobic metabolism. They mainly include superoxide anion, hydrogen peroxide, hydroxyl radicals, singlet oxygen, ozone, and nitric oxide and are implicated in many physiological and pathological processes. Bilirubin, a cardinal pigment in the bile, has been increasingly investigated to treat cancer, diabetes, ischemia–reperfusion injury, asthma, and inflammatory bowel diseases (IBD). Indeed, bilirubin has been shown to eliminate ROS production, so it is now considered as a promising therapeutic agent for ROS-mediated diseases and can be used for the development of antioxidative Nanomedicines.



Graphical abstract

Bilirubin-derived nanoparticles (BRNPs) have shown promising therapeutic and diagnostic effects in numerous diseases via their antioxidant, immunomodulatory, metabolic-modulating and antiproliferative effects.



Bilirubin is a common yellowish pigment derived from hemoglobin thatis insoluble in water and soluble in alkali, benzene, chloroform, and other organic solvents.

Molecular Formula-(C33H36N4O6)

Reactive oxygen species (ROS) are highly reactive molecules that are constantly generated as byproducts of normal cellular metabolism. While ROS play essential roles in various physiological processes, such as cell signaling and immune response, their excessive production can lead to oxidative stress, which is implicated in the pathogenesis of numerous diseases. ROS-mediated damage has been linked to conditions including neurodegenerative disorders, cardiovascular diseases, cancer, and inflammatory diseases, among others. Developing effective strategies to mitigate ROS-induced damage and cellular homeostasis is a major focus of current research in the field of nanomedicine.

In recent years, nanotechnology has emerged as a promising approach for the delivery of therapeutic agents, owing to its unique properties and versatility. Nanomedicines, which encompass a wide range of nanoscale formulations, offer several advantages for the treatment of ROS-mediated diseases. Among these, bilirubin-based nanomedicines have garnered significant attention due to their inherent antioxidant properties and potential therapeutic applications. Bilirubin, a yellow tetrapyrrolic pigment derived from the breakdown of heme, has long been recognized for its role inthe detoxification of ROS. It possesses potent antioxidant and anti- inflammatory properties, making it an ideal candidate for developing nanomedicines aimed at combating ROS-induced damage.

Whether ROS act as damage molecules or signal molecules depends on the concentration of ROS in living organisms, which is associated with the endogenous antioxidant-protective systems. Therefore, research onthe regulation of ROS concentration has caused wide concern, mainly involving the topics in ROS-regulating therapy such as antioxidant therapy triggered by ROS scavengers and ROS-induced toxic therapy mediated by ROS-elevation agents (e.g., photosensitizers (PSs)).
Currently, ROS-regulating researches have achieved great development,offering reasonable explanations on the physiological and pathological roles of ROS.[5, 20-22] In particular, over the past few decades, nanoscience and nanotechnology are introduced in ROS-regulating study, further accelerating their fast development. ROS research with the assistance of nanotechnology is mainly reflected in the development of ROS-related nanomedicines or nontherapeutic modalities. Here, these ROS-based Nano therapeutic modalities or nanomedicines that can regulate ROS progress depend on the intrinsic biophysical and biochemical characteristics of nanomaterials, such as their appropriate sizes (usually 10–100 nm), many interface/surface options and high specific surface area.

The employment of nanomaterials in ROS-regulating therapy exhibitsvarious advantages such as improved stability and biocompatibility of ROS-regulating agents, enhanced drug accumulation, optimized pharmacokinetics.

Conclusion :

Over the few decades, nanoscience and nanotechnology are introduced in ROS-regulating study, further accelerating their fast development. ROS research with the assistance of nanotechnology is mainly reflected in the development of ROS-related nanomedicine. Due to it's Anti oxidant therapy triggered by ROS scavenger & mediated ROS elevation agent.

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