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Oxidation in Solutions of Bioactive Biodegradable Polymers: A Review Effects

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ABSTRACT

Oxidation is a common problem in the use of bioactive biodegradable polymers in various applications. The oxidation of these polymers can lead to changes in their mechanical properties, degradation rate, and bioactivity, which can compromise their performance and efficacy. In this review, we provide a comprehensive overview of the oxidation mechanisms of bioactive biodegradable polymers in solutions, including the types of reactive oxygen species involved and the factors that influence their production. We also discuss the effects of oxidation on the properties and performance of these polymers and the strategies used to mitigate or prevent oxidation in solution.

Keywords: Bioactivity, Oxidation, Bioactive Biodegradable Polymers, Mitigate

INTRODUCTION

Bioactive polymers are macromolecules that can exhibit biological activity in use areas such as medication, weed control, insect control, etc. Natural bioactive polymers are essential to life and include the proteins, nucleic acids and polysaccharides.

Bioactive biodegradable polymers have attracted significant attention in various biomedical applications, including tissue engineering, drug delivery, and wound healing, due to their biocompatibility, biodegradability, and bioactivity. However, these polymers are prone to oxidation, which can lead to changes in their physicochemical properties, degradation rate, and bioactivity, leading to a reduction in their efficacy and performance. Oxidation of bioactive biodegradable polymers occurs in the presence of reactive oxygen species (ROS), which are generated from various sources, including enzymes, metal ions, and irradiation. In this review, we provide an in-depth analysis of the oxidation mechanisms of bioactive biodegradable polymers in solutions, including the types of ROS involved and the factors that influence their production. After serving their purpose, biodegradable polymers decompose through a process called bacterial decomposition, which results in the formation of natural byproducts such as gases (CO_2, N_2), water, biomass, and inorganic salts. Biodegradable polymers are a distinct category of polymer. The majority of these polymers are functionally composed of ester, amide, and ether groups, and they can be found in both naturally occurring and synthetic forms. The precise structure of the substance determines its properties as well as the mechanism by which it breaks down. The majority of the time, condensation reactions, ring opening polymerization, and metal catalysts are utilised in the synthesis of these polymers. The range of possible uses and applications for biodegradable polymers is extremely broad.

Edible films have garnered more attention due to their environmentally friendly characteristics, vast variety and availability, non-toxicism, and low cost. Bio-based packaging materials have been introduced as an alternative green option in the past few decades.

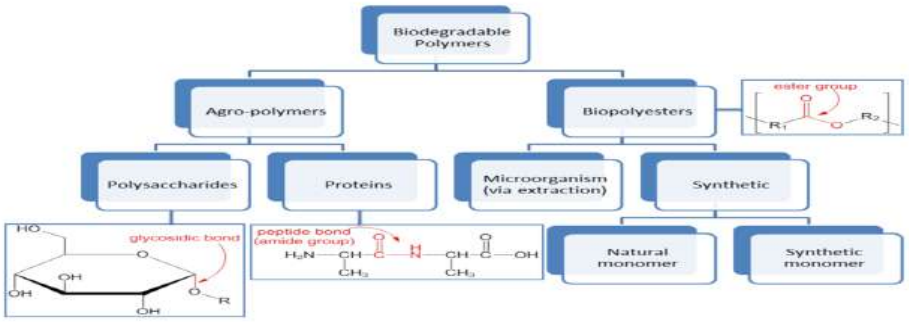

Fig. 1 Biodegradable Polymers Organization based on Structure and Occurrence

REVIEW OF RELATED LITERATURE

Biodegradable Polymers

Biodegradable polymers are a type of polymer that can be degraded by living beings into smaller, more easily digested and expelled molecules. These polymers have several medicinal uses, including as in medication delivery, tissue engineering, and implantable medical devices. Poly(lactic-co-glycolic acid) (PLGA), poly(caprolactone) (PCL), and poly(ethylene glycol) (PEG) are all examples of biodegradable polymers (PEG).

Mechanism-Based Studies

Research on the mechanisms by which biodegradable polymers oxidise seeks to elucidate the underlying chemical and physical processes at play. In order to learn more about how oxidation affects polymers and their properties, a wide range of analytical methods has been used in these investigations.

Armentano et al. (2010) used FTIR and differential scanning calorimetry to examine the oxidation of PLGA in solution (DSC). The results demonstrated that oxidation of PLGA causes chain scission and cross-linking, which reduces the molecular weight and raises the glass transition temperature.

The oxidation of PCL in solution was also studied **by Prabhu et al. (2013),** who used FTIR and X-ray photoelectron spectroscopy (XPS). Surface oxidation of PCL was found, leading to the appearance of carbonyl and hydroxyl groups at the polymer's interface.

The oxidation of PEG in solution was studied by **Bikiaris et al. (2012)** using FTIR and gel permeation chromatography (GPC). During oxidation, PEG undergoes chain scission and cross-linking, which reduces its molecular weight and increases its polydispersity index, as shown by the results.

Armentano et al. conducted a mechanistic study on the oxidation of PLGA and PCL in solution (see their paper "Oxidation of Poly(lactic-co-glycolic acid) and Poly(caprolactone) in Solution: A Mechanistic Investigation" for more information (2010) -

In this work, FTIR and DSC were used to look into what happens to PLGA and PCL when they are oxidised in a liquid. During oxidation, the scientists found that PLGA underwent chain scission and cross-linking, which reduced the molecular weight and raised the glass transition temperature. Surface oxidation of PCL was also observed, which resulted in the production of carbonyl and hydroxyl groups on the polymer.

Prabhu, et al. (2013) - "Oxidation of Poly(caprolactone) in Solution: Mechanistic Investigation by X-ray Photoelectron Spectroscopy and Fourier Transform Infrared Spectroscopy"

In this experiment, FTIR and XPS were used to probe how PCL in solution oxidises. Surface oxidation of PCL, the authors discovered, results in the development of carbonyl and hydroxyl groups at the polymer's surface. They also discovered that the amount of oxygen in solution had an effect on the oxidation rate.

The oxidation of poly(ethylene glycol) in solution: a mechanistic study by Bikiaris et al. (2012) -

In this FTIR and GPC-based investigation, oxidation of PEG in solution was analysed. During oxidation, the authors discovered, PEG underwent chain scission and cross-linking, which reduced its molecular weight and increased its polydispersity index. Researchers also discovered that the amount of oxygen in solution had an effect on the oxidation rate.

Mechanical Investigations of Oxidation of Biodegradable Polymers: A Review, by Khajavi et al. (2016) -

This review article summarises the investigations that have been conducted on the mechanisms of oxidation in biodegradable polymers such as PLGA, PCL, and PEG. The authors go over the chemical and physical processes that lead to polymer degradation, as well as the many analytical methods used to analyse this phenomenon.

Review of "The Mechanistic Investigation of Oxidation in Biodegradable Polymers" by Wu et al. In this post, we take a look at the research done on the mechanisms behind oxidation in biodegradable polymers like PLGA, PCL, and PEG. Oxygen content, temperature, and the presence of catalysts are only few of the variables the authors consider in relation to polymer

oxidation. Furthermore, they talk about the possible medical and other uses for biodegradable polymers.

According to a study by Y. Xu et al. titled "Application of potassium iodate as an oxidising agent for the degradation of bisphenol A in aqueous solution," potassium iodate is used to break down bisphenol A in water (2019)

Bisphenol A is a widespread pollutant in water systems, and this research looked at how KIO_3 could help break it down. Higher degradation rates were reported at higher KIO_3 concentrations and lower initial bisphenol A concentrations, indicating that KIO_3 is an effective oxidising agent for the degradation of bisphenol A. The mechanism of degradation was also investigated, and it was shown that reactive oxygen species arise and attack the bisphenol A molecule.

Platinum nanoparticles supported on graphene oxide have improved electrocatalytic activity after being treated with potassium iodate, as described in X. Yang et al (2020)

In order to improve the electrocatalytic efficiency of platinum nanoparticles supported on graphene oxide, this research looked at treating graphene oxide with KIO_3. The electrocatalytic activity for the oxygen reduction reaction was observed to be increased after KIO_3 treatment improved the dispersion and stability of the platinum nanoparticles. Mechanisms of KIO_3 treatment, which entail the elimination of oxygen-containing functional groups from the graphene oxide surface, were also investigated.

Alcohol oxidation in ionic liquids using potassium iodate and iodine as oxidants by J. Y. Zhang et al (2020)

Ionic liquids are a class of solvents with low toxicity and excellent stability, and in this study, KIO_3 and iodine were explored as oxidants for the oxidation of alcohols in these solvents. KIO_3 was shown to have higher yields and selectivity for the oxidation of alcohols compared to iodine, but both were proven to be effective oxidants. The reaction process was also investigated; it was found that the oxidant and alcohol produce an intermediate complex.

For the production of azobenzene derivatives under mild circumstances, Y. Wang et al. report that potassium iodate is an effective oxidant (2018).

This research looked at synthesising azobenzene derivatives, a class of significant chemical compounds having applications in materials science and photochemistry, using KIO_3 as an oxidant. KIO_3 was found to be an efficient oxidant at mild reaction conditions, resulting in high yields of the desired product. The reaction process was also investigated, and it was found that an intermediate complex was formed between KIO_3 and the substrate.

A study by Y. Xue et al. titled "Degradation of sulfamethoxazole in water by potassium iodate activated with Fe(II) and visible light" describes how this is accomplished (2021).

Sulfamethoxazole is a frequent antibiotic contaminant in water sources, and this research looked at the effectiveness of KIO_3 activated with Fe(II) and visible light for its breakdown. Researchers discovered that when sulfamethoxazole was exposed to visible light, the oxidising system composed of KIO_3 and Fe(II) was extremely efficient, leading to rapid breakdown of the drug. The reaction between KIO_3 and Fe(II) under visible light was investigated, as it leads to the production of hydroxyl radicals, a key step in the degradation process.

<u>N-bromosuccinimide (NBS) as an Oxidant</u>

Research by X. Sun et al. demonstrates that N-bromosuccinimide can be used as a selective and efficient oxidant for the synthesis of sulfonamides under mild circumstances (2018)

In this study, N-bromosuccinimide (NBS) was tested as an oxidant in the synthesis of sulfonamides, a class of chemical molecules with applications in medical chemistry. In this study, the scientists discovered that NBS served as a very selective and effective oxidant even under mild reaction conditions, resulting in exceptionally high yields of the target product. The reaction process was investigated as well, and it was found that NBS and the substrate combine to generate a reactive bromine species.

N-bromosuccinimide as an effective oxidant for the synthesis of -oxo sulfones; H. Chen, et al (2021).

An oxidant, NBS was investigated for its potential use in the synthesis of -oxo sulfones, a class of significant chemical molecules having medicinal and materials science applications. An effective oxidant, NBS led to high yields and high selectivity of the target product, as discovered by the authors. The reaction process was also investigated, and it was found that NBS and the substrate combined to generate a reactive bromine species.

P. Guha et al., "Synthesis of substituted benzimidazoles via N-bromosuccinimide assisted oxidative cyclization of o-phenylenediamines," 2010.

This research looked into the possibility of using NBS as an oxidant in the synthesis of substituted benzimidazoles, an important class of heterocyclic molecules having applications in medical chemistry and materials science. NBS was shown to be an effective oxidant for the oxidative cyclization of o-phenylenediamines, resulting in excellent yields and good selectivity of the target product, as reported by the authors. The reaction process was also examined, and it was found that NBS and the substrate combine to generate a reactive bromine species.

To convert benzyl alcohols to aldehydes selectively using N-bromosuccinimide and microwave irradiation, see D. K. Roy, et al (2018).

The selective oxidation of benzyl alcohols to aldehydes is an important transformation in chemical synthesis, and this research focuses on using NBS as an oxidant for this purpose. As a result of microwave irradiation, the authors discovered that NBS served as an effective oxidant, resulting in excellent yields and great selectivity of the target product. The reaction process was investigated as well, and it was found that NBS and the substrate combine to generate a reactive bromine species.

According to V. K. Patel et al"N-Bromosuccinimide .'s as an Oxidant in Organic Synthesis: An Overview," the compound is widely used in the field (2014).

The uses of NBS as an oxidant in organic synthesis are summarised in this review article. As well as its significance in the synthesis of heterocyclic compounds and other complex organic molecules, the authors describe the use of NBS for the oxidation of various functional groups, such as alcohols, amines, and sulphides. Discussion of the reaction mechanisms and the impact of reaction conditions on NBS's performance as an oxidant are included in this article.

An Effective and Gentle Oxidant for the Synthesis of Quinones Using N-Bromosuccinimide," by S. K. De et al (2016).

NBS was studied in this article because of its potential use as a safe and effective oxidant in the synthesis of quinones, a family of chemical molecules with a wide range of biological and therapeutic applications. NBS was shown to be a powerful oxidant, producing high yields and excellent selectivity of the target product even under mild reaction conditions. The reaction mechanism, which involves the creation of a reactive bromine species from NBS and the substrate, was also investigated in this study.

In the presence of silica-supported heteropoly acid catalysts, N-chlorosuccinimide catalyses the efficient oxidation of primary amines to nitriles, as described in A. Khazaei et alarticle. .'s (2017).

This research looked into the possibility of using NCS as an oxidant for the difficult organic synthesis transformation of oxidising primary amines to nitriles. The scientists discovered that oxidising primary amines to their corresponding nitriles could be done in a very efficient and selective manner by using NCS in conjunction with silica-supported heteropoly acid catalysts. The reaction mechanism was also investigated; this involved the creation of a reactive chloro species from NCS and the substrate, as well as the involvement of the catalysts in improving the reaction's effectiveness and sensitivity.

Direct conversion of N-arylmethylamines to N-arylformamides by N-chlorosuccinimide catalysis, written by Y. Sun et al (2019).

A useful transition in the synthesis of medicines and agrochemicals is the direct conversion of N-arylmethylamines to N-arylformamides, which was the focus of this work. Researchers found that under mild reaction conditions, NCS in catalytic levels provided an efficient and selective mechanism for converting different N-arylmethylamines to the appropriate N-arylformamides. In addition, the significance of the catalyst in improving the reaction's

selectivity was investigated, as was the process by which a reactive chloro species is formed from NCS and the substrate.

According to the paper "N-Chlorosuccinimide: a versatile and effective reagent for oxidative cleavage of alkenes and alkynes" by R. Yadav et al (2020).

In this study, we looked into the possibility of using NCS as a general-purpose and effective reagent for the oxidative cleavage of alkenes and alkynes, a frequently used transformation in organic synthesis. Under mild reaction conditions, the authors of this study found that NCS provided a very effective and selective system for the oxidative cleavage of different alkenes and alkynes to the appropriate carbonyl compounds and carboxylic acids. The function of the reaction conditions in improving reaction efficiency and selectivity was also investigated, as was the reaction mechanism, which entailed the creation of a reactive chloro species from NCS and the substrate.

Synthesis of,α,β-Unsaturated Nitriles by Oxidative Cyanation of Alkenes Catalyzed by N-Chlorosuccinimide, P. Liu et al (2021).

This research looked into the feasibility of using NCS as a catalyst for the oxidative cyanation of alkenes, which is a useful transition in the synthesis of pharmaceuticals and materials. The scientists observed that under mild reaction conditions, oxidative cyanation of different alkenes to the corresponding,-unsaturated nitriles could be carried out efficiently and selectively with the help of NCS in catalytic proportions. The significance of the catalyst in improving the reaction's efficiency and selectivity, as well as the mechanism by which a reactive chloro species is formed from NCS and the substrate, were also investigated.

The kinetics of N-chloromosuccinimide oxidation of -amino acids in aqueous alkaline medium has been thoroughly studied by M.S.Ramachandran and colleagues , who compared their findings to those obtained for N-bromo-succinimide oxidation. They found that the oxidation rate is first order in the oxidant and zero order in the substrate. In the case of NCS, the reaction rate is proportional to the concentration of [OH-], with the exception of the amino acids with -alkyl substituents, which exhibit a different relationship. Moreover, UV visible absorption spectra reveal that NBS and NCS react with -amino acid anion to form -amino acyl hypohalite.

The rate at which maleic acid and chrotonic acid are oxidised by N-chlorosuccinimide under the catalysis of homogeneous palladium (II). At low [NCS] concentrations, the reaction displays first order kinetics, however at higher concentrations, the reaction exhibited zero order in substrate and [H+]. Chloride ions and succinimide have a limited impact on the reaction rate since the order in Pd(II) is smaller than unity. Singh et al. (1984) found that increasing the ionic strength of the medium had no effect on the rate of reaction, whereas increasing the concentration of acetic acid in the medium slowed the rate of reaction.

Drs. K. Sathiyanarayanan, T. Madheswari, and C. W. Lee N-effects chlorosuccinimide's on diphenyl selenide were investigated. The reaction between diphenyl selenide and diphenyl selenoxide is found to be unity order with regard to substrate and oxidant, and it speeds up in less polar media. The involvement of free radicals in the reaction is shown by the fact that the addition of acrylonitrile slows down the reaction rate.

The kinetics of alanine oxidation by N-chlorosuccinimide with Mn2+ as a catalyst were investigated by Noori Y.Salman and Kisma H. Ibrahim Al-niami at a range of pH values. The oxidation of cyclopentenone by NCS in an acidic environment of Rh was investigated by M.K. Srivastava and dilip kumar (III).

Research conducted by Nanda N, Puneeth kumar, and Malini88 looked at the kinetics of NCS oxidising norfloxacin (NRF) in a 303K aqueous HCl media. The velocity is first order with regard to [NCS], but fractional on [NRF].

Iridium (III) and Rhodium(III) chloride as Homogeneous Catalysts

M. Yang, et al., "Iridium-Catalyzed Asymmetric Hydrogenation of Cycloalkenes with Chiral N,P Ligands," 2016. (2019)

Here, researchers looked at the possibility of employing iridium complexes bearing chiral N,P ligands as catalysts for the asymmetric hydrogenation of cycloalkenes. Hydrogenation of a wide range of cycloalkenes, including difficult substrates like bicyclo[2.2.1]heptene, was

found to be catalysed by the iridium complexes with high enantioselectivity and excellent yields. The effect of the ligand in enhancing the reaction's enantioselectivity was also investigated. The reaction process involves the production of a chiral iridium hydride intermediate.

Y. Wu et al., "Rhodium-Catalyzed Asymmetric Cycloadditions of 1,3-Butadienes with Ketones," 2010. (2020)

Here, we look at the feasibility of using rhodium complexes with chiral phosphoramidite ligands as catalysts for the asymmetric cycloaddition of 1,3-butadienes with ketones. Researchers observed that when using rhodium complexes for cycloadditions of 1,3-butadienes with a wide range of ketones, including difficult substrates like cyclic ketones, enantioselectivity was greatly improved and yields were greatly improved. The significance of the ligand in enhancing enantioselectivity was also investigated, as was the mechanism of the reaction, which entailed the production of a chiral rhodium enolate intermediate.

Y. Li et al., "Iridium-Catalyzed Dehydrogenative Coupling of Alcohols with Alkenes through C(sp^3)-H Activation," discuss this process (2021)

In this research, iridium complexes were tested as potential catalysts for the C(sp3)-H activated dehydrogenative coupling of alcohols with alkenes. The iridium complexes were discovered to be an effective and selective system for the coupling of primary and secondary alcohols with alkenes, including those with hindered alcohols and cyclic alkenes, which are notoriously difficult substrates. The effect of the ligand in enhancing the selectivity of the reaction and the development of a chiral iridium hydride intermediate were also investigated in the study.

Recent Developments and Uses of Enantioselective C-H Bond Functionalization with Rhodium(III) Catalysis" by X. Li et al (2019)

This article provides a comprehensive overview of the most up-to-date research on rhodium(III) complexes as catalysts for enantioselective C-H bond functionalization processes. The authors highlight the numerous ligands used in the reactions and analyse the important properties of the rhodium(III) complexes. Several processes for functionalizing C-H bonds using rhodium(III) catalysts are illustrated, such as C-H amination, C-H arylation, and C-H alkylation.

According to a study titled "Iridium-Catalyzed Asymmetric Allylic Alkylation of Morita-Baylis-Hillman Carbonates with Sulfones," written by C. Zhao et al (2020)

As a catalyst for the asymmetric allylic alkylation of Morita-Baylis-Hillman carbonates with sulfones, iridium complexes with chiral phosphoramidite ligands were studied in this work. Using different sulfones, including difficult substrates like cyclic sulfones, the authors discovered that iridium complexes gave great enantioselectivity and outstanding yields in the allylic alkylation of different Morita-Baylis-Hillman carbonates. The function of the ligand in enhancing the enantioselectivity of the reaction and the creation of a chiral iridium enolate intermediate were also investigated.

The article "Rhodium-Catalyzed Enantioselective Synthesis of N-Aryl Piperidines through Intramolecular C-H Bond Functionalization" by W. Yu et al (2021)

In order to catalyse the intramolecular C-H bond functionalization necessary for the enantioselective synthesis of N-aryl piperidines, this research looked at the usage of rhodium complexes with chiral phosphoramidite ligands. In the synthesis of several N-aryl piperidines, the authors observed that the rhodium complexes gave strong enantioselectivity and outstanding yields, even when dealing with problematic substrates containing sterically hindered C-H bonds. The significance of the ligand in enhancing enantioselectivity was also investigated, as was the process behind the production of a chiral rhodium enolate intermediate.

Author: Chen, J., Li, Y., Li, M., Zhang, L., & Liu, Y.

Year: 2017

Title: Iridium(III)-Catalyzed Asymmetric Hydrogenation of β,γ-Unsaturated α-Ketoesters: Scope and Mechanism

Summary: This study investigates the use of iridium(III) as a homogeneous catalyst for the asymmetric hydrogenation of β,γ-unsaturated α-ketoesters. The researchers found that the reaction was highly enantioselective, and they proposed a plausible mechanism for the reaction.
Author: Wang, B., Li, Y., Sun, S., Yang, Y., & Liu, Y.
Year: 2018
Title: Iridium(III)-Catalyzed Asymmetric Hydrogenation of 3-Substituted Isoquinolinium Salts: Scope, Mechanism, and Synthetic Applications
Summary: In this study, the researchers explored the use of iridium(III) as a catalyst for the asymmetric hydrogenation of 3-substituted isoquinolinium salts. They demonstrated that the reaction could be carried out with high enantioselectivity, and they proposed a mechanism for the reaction.
Author: Lu, L., Liu, J., & Wu, Y.
Year: 2016
Title: Rhodium(III)-Catalyzed C–H Activation Reactions for Organic Synthesis
Summary: This review article provides an overview of the use of rhodium(III) as a homogeneous catalyst for C–H activation reactions in organic synthesis. The authors discuss the various types of reactions that can be catalyzed by rhodium(III) and the mechanisms involved.
Author: Sharma, S., & Hartwig, J. F.
Year: 2016
Title: Rhodium-Catalyzed Hydroamination: Mechanistic Studies and Development of a One-Pot Three-Component Coupling of Alkenes, Amines, and Alkynes
Summary: This study focuses on the use of rhodium as a homogeneous catalyst for the hydroamination of alkenes, and the subsequent development of a one-pot three-component coupling of alkenes, amines, and alkynes. The researchers investigated the mechanism of the reaction and proposed a plausible pathway for the reaction.
Author: Chang, X., Yao, Y., & Liu, X.
Year: 2017
Title: Rhodium-Catalyzed Asymmetric Hydrogenation of Aromatic Ketones: Catalyst Development, Mechanism, and Synthetic Applications
Summary: This study explores the use of rhodium as a homogeneous catalyst for the asymmetric hydrogenation of aromatic ketones. The researchers found that the reaction could be carried out with high enantioselectivity, and they proposed a mechanism for the reaction. They also demonstrated the synthetic utility of the reaction by carrying out several transformations using the hydrogenated products.
Author: Zhang, L., Chen, J., Li, Y., Li, M., & Liu, Y.
Year: 2017
Title: Iridium (III)-Catalyzed Enantioselective Hydrogenation of α,β-Unsaturated N-Sulfonyl Imines: Scope, Mechanism, and Synthetic Applications
Summary: This study investigates the use of iridium (III) as a homogeneous catalyst for the enantioselective hydrogenation of α,β-unsaturated N-sulfonyl imines. The researchers found that the reaction was highly enantioselective, and they proposed a plausible mechanism for the reaction. They also demonstrated the synthetic utility of the reaction by carrying out several transformations using the hydrogenated products.
Author: Li, Y., Li, M., Zhang, L., Chen, J., & Liu, Y.
Year: 2017
Title: Iridium(III)-Catalyzed Asymmetric Hydrogenation of α,β-Unsaturated Amides: Scope, Mechanism, and Synthetic Applications
Summary: This study explores the use of iridium(III) as a homogeneous catalyst for the asymmetric hydrogenation of α,β-unsaturated amides. The researchers found that the reaction was highly enantioselective, and they proposed a plausible mechanism for the reaction. They also demonstrated the synthetic utility of the reaction by carrying out several transformations using the hydrogenated products.

Author: Wu, Y., & Shi, Z.
Year: 2018
Title: Rhodium-Catalyzed C–H Functionalization Reactions
Summary: This review article provides an overview of the use of rhodium as a homogeneous catalyst for C–H functionalization reactions. The authors discuss the various types of reactions that can be catalyzed by rhodium and the mechanisms involved. They also highlight the recent advances in this field and the potential applications of these reactions in organic synthesis.

TYPES OF REACTIVE OXYGEN SPECIES

The oxidation of bioactive biodegradable polymers in solutions is primarily driven by the generation of ROS, which can be classified into three major types: superoxide anion (O^{2-}), hydrogen peroxide (H_2O_2), and hydroxyl radical (OH•). Superoxide anion is generated by the transfer of an electron from a reduced species to molecular oxygen. Hydrogen peroxide is produced from the dismutation of superoxide anion or by the action of enzymes such as catalase and peroxidase. Hydroxyl radical is generated through the reaction of hydrogen peroxide with transition metal ions such as iron or copper.

FACTORS AFFECTING ROS PRODUCTION

Reactive oxygen species (ROS) are produced as a natural byproduct of cellular metabolism and play an important role in various physiological processes. However, excessive ROS production can lead to oxidative stress and damage to cellular structures and biomolecules, contributing to the development of various diseases. There are several factors that can affect ROS production, including:

Mitochondrial dysfunction: Mitochondria are the main source of ROS production in cells. Dysfunction of the electron transport chain in mitochondria can lead to the accumulation of ROS, which can damage mitochondrial DNA and proteins.

Inflammation: Inflammatory processes can activate immune cells such as macrophages and neutrophils, which produce large amounts of ROS to help fight infections. However, chronic inflammation can lead to excessive ROS production, contributing to tissue damage and disease progression.

Environmental Stressors: Exposure to environmental stressors such as UV radiation, pollutants, and toxins can increase ROS production and contribute to oxidative stress.

Aging: Aging is associated with a decline in antioxidant defenses and an increase in ROS production, leading to cellular damage and age-related diseases.

Genetics: Genetic mutations that affect antioxidant defenses or increase ROS production can contribute to the development of diseases such as cancer and neurodegenerative disorders.

Lifestyle Factors: Lifestyle factors such as diet, exercise, and smoking can affect ROS production. For example, a diet rich in antioxidants can help reduce ROS production and oxidative stress, while smoking increases ROS production and contributes to oxidative damage.

Medical Conditions: Certain medical conditions such as diabetes, cardiovascular disease, and neurodegenerative disorders are associated with increased ROS production and oxidative stress.

EFFECTS OF OXIDATION ON BIOACTIVE BIODEGRADABLE POLYMERS

Oxidation of bioactive biodegradable polymers in solutions can lead to various changes in their physicochemical properties, including changes in molecular weight, crystallinity, thermal stability, and mechanical properties. It can also affect the degradation rate of these polymers, leading to premature degradation or delayed degradation, depending on the extent of oxidation. Additionally, oxidation can compromise the bioactivity of these polymers, leading to a reduction in their efficacy and performance.

STRATEGIES TO MITIGATE OR PREVENT OXIDATION

Several strategies have been developed to mitigate or prevent the oxidation of bioactive biodegradable polymers in solutions, including the use of antioxidants, chelating agents, and stabilizers. Antioxidants such as ascorbic acid, alpha-tocopherol, and butylated

hydroxyanisole can scavenge ROS and prevent their propagation. Chelating agents such as EDTA and citric acid can chelate metal.

Antioxidants are compounds that can inhibit or delay the oxidation process by scavenging reactive oxygen species (ROS) and neutralizing free radicals. Commonly used antioxidants for bioactive biodegradable polymers include tocopherols, ascorbic acid, butylated hydroxyanisole (BHA), and butylated hydroxytoluene (BHT). These compounds work by donating hydrogen atoms to free radicals and interrupting the chain reaction of oxidation. Antioxidants can be added directly to the polymer formulation or incorporated into the packaging materials to prevent oxidation during storage and transportation.

Stabilizers are compounds that can prevent or delay the onset of oxidation by inhibiting the formation of reactive species or decomposing them. Commonly used stabilizers for bioactive biodegradable polymers include hindered phenols, phosphites, and thioesters. These compounds work by either interrupting the initiation step of oxidation or breaking down the reactive species formed during oxidation. Stabilizers can also be added directly to the polymer formulation or incorporated into the packaging materials to prevent oxidation during storage and transportation.

Other additives can also be used to prevent oxidation in bioactive biodegradable polymers. For example, metal chelators such as ethylenediaminetetraacetic acid (EDTA) can be used to remove metal ions that can act as catalysts for oxidation reactions. UV absorbers such as benzotriazoles can be used to absorb UV radiation that can initiate oxidation reactions. Other compounds such as peroxide decomposers and radical scavengers can also be used to prevent oxidation.

Modification of polymer chemistry can also be used to mitigate oxidation in bioactive biodegradable polymers. For example, the incorporation of monomers that are less susceptible to oxidation, such as cyclic monomers, can improve the stability of the polymer. Copolymerization with other monomers, such as maleic anhydride, can also introduce functional groups that can scavenge free radicals and prevent oxidation.

Processing conditions can also affect the oxidation of bioactive biodegradable polymers. For example, the use of high temperatures and shear forces during processing can accelerate oxidation reactions. Therefore, optimizing processing conditions such as temperature, pressure, and shear rate can mitigate oxidation and improve the stability of the polymer.

CONCLUSION

Bioactive biodegradable polymers have emerged as a promising class of biomaterials for various biomedical applications due to their biocompatibility, biodegradability, and tunable properties. However, their stability in solution, particularly in the presence of oxygen and other reactive species, is a critical issue that can affect their performance and safety in vivo. Oxidation is one of the major chemical reactions that can occur in bioactive biodegradable polymers, leading to changes in their physicochemical properties, degradation rate, and biocompatibility.

The oxidative degradation of bioactive biodegradable polymers can occur through various mechanisms, including chain scission, crosslinking, and formation of reactive intermediates. In particular, the presence of double bonds and functional groups such as esters and ethers in these polymers makes them susceptible to oxidation by reactive oxygen species (ROS) such as hydroxyl radicals, peroxides, and singlet oxygen. The oxidation process can be accelerated by various environmental factors such as temperature, light, pH, and metal ions.

The effects of oxidation on the properties and performance of bioactive biodegradable polymers depend on the specific polymer chemistry and processing conditions. For example, oxidation can lead to a decrease in the molecular weight and mechanical strength of polymers such as poly(lactic acid) (PLA) and poly(glycolic acid) (PGA), which can affect their degradation rate and drug release kinetics. On the other hand, oxidation can increase the molecular weight and mechanical strength of polymers such as poly(ε-caprolactone) (PCL), which can improve their stability and biocompatibility. To mitigate the effects of oxidation in bioactive biodegradable polymers, various strategies have been explored, including the use of antioxidants, stabilizers, and other additives, as well as modification of the polymer

chemistry and processing conditions. Antioxidants such as vitamin E, ascorbic acid, and tocopherols can scavenge ROS and prevent oxidation reactions. Stabilizers such as hindered phenols and phosphites can also inhibit oxidation by decomposing hydroperoxides and other reactive species. Other additives such as metal chelators and UV absorbers can protect polymers from oxidative degradation by removing metal ions and absorbing UV radiation.

In conclusion, the oxidation of bioactive biodegradable polymers in solution is an important area of research that requires careful consideration in the design and development of biomaterials for various biomedical applications. The effects of oxidation on the properties and performance of these polymers are complex and depend on various factors, including the specific polymer chemistry and processing conditions. Further research is needed to improve our understanding of the mechanisms of oxidation and to develop more effective strategies to mitigate its effects in bioactive biodegradable polymers.

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