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REVEIEW ARTICLE

Astaxanthin as a potential therapeutic agent for knee osteoarthritis: A review of mechanisms and clinical evidence

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Abstract

Bakground: Knee osteoarthritis (KOA) poses an important challenge in musculoskeletal healthcare, prompting the need for innovative therapeutic strategies. Astaxanthin, a potent antioxidant carotenoid, has gained interest due to its multifaceted mechanisms of action and potential role in KOA management. This review aims to examine the therapeutic mechanisms of astaxanthin in KOA, alongside clinical evidence supporting its effectiveness through a narrative synthesis of preclinical and clinical studies.

Methods: A comprehensive review of the literature was conducted across Web of Science, Pubmed, Scopus and Google Scholar, focusing on studies that explored astaxanthin's antioxidative, anti-inflammatory, and cartilage-protective properties in the context of KOA. Articles published in English between 2014 and 2024 were included (n=44).

Results: The review identified several key mechanisms by which astaxanthin exerts its therapeutic effects, including reducing oxidative stress, attenuating inflammation, and preserving cartilage integrity. Clinical studies also provided promising evidence of its efficacy in alleviating symptoms and improving joint function in patients with KOA.

Conclusion: Astaxanthin demonstrates considerable potential as a therapeutic agent for KOA, though further research is needed to fully understand its long-term efficacy and optimal dosing. Future studies should focus on refining methodological approaches to better elucidate astaxanthin's role in KOA management.

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Key messages

Astaxanthin, a powerful antioxidant, shows promise in managing knee osteoarthritis by reducing pain, inflammation, and cartilage degradation. It modulates key inflammatory pathways and strengthens antioxidant defenses, offering symptom relief and potential disease modification. Future research should focus on optimizing dosages, exploring long-term effects, and testing combination therapies.

Introduction

Knee osteoarthritis (KOA) stands as a prevalent and burdensome musculoskeletal ailment characterized by the gradual degradation of cartilage, accompanied by inflammation and debilitating pain.[1] The global prevalence of KOA underscores its significant influence on healthcare systems, necessitating effective treatment strategies. Nevertheless, existing therapeutic approaches for KOA often prioritize symptom management over disease modification, leaving a critical gap in addressing the underlying pathophysiology.[2] Subsequently, there is a growing impetus to explore alternative treatments, particularly natural compounds, with the potential to mitigate the progression of KOA and improve patient outcomes.[3] Among these compounds, astaxanthin, a xanthophyll carotenoid abundant in algae, seafood, and also select plants, has garnered considerable attention for its multifaceted therapeutic properties, including potent antioxidative, anti-inflammatory, and also cartilage-protective effects.[4]

Mechanical factors, such as obesity, excessive joint use, and poor muscle strength, along with anatomic factors like joint shape and alignment abnormalities, contribute significantly to the development of KOA. Genetic predispositions and inflammatory processes further exacerbate cartilage degradation and joint dysfunction.[5] As researchers increasingly recognize the potential of astaxanthin in KOA management, there arises a need for a comprehensive review elucidating its mechanisms of action, efficacy in preclinical and clinical studies, safety profile, and avenues for future research. [5]Thus, this review endeavors to provide an extensive exploration of astaxanthin as a promising therapeutic agent for KOA, targeting to inform and guide further advancements in the field of osteoarthritis management.

Methods

Study selection criteria

A comprehensive search was conducted across databases such as Web of Science, PubMed, Scopus, and Google Scholar, focusing on peer-reviewed articles published between 2014 and 2024 regarding the therapeutic potential of astaxanthin in knee osteoarthritis (KOA). The search utilized specific terms related to astaxanthin and KOA, encompassing both preclinical and clinical studies. Predefined inclusion criteria ensured relevance, including studies on astaxanthin supplementation in KOA, full-text availability, and publication in English. Out of 68 initially identified studies, 44 were selected based on these criteria for further analysis.

Data extraction

Data extraction was performed systematically from the 44 selected studies to gather essential information on astaxanthin's effects on KOA. Key details included study design, sample size, dosage and duration of supplementation, and primary outcomes measured. Focus was placed on astaxanthin's mechanisms of action, efficacy, and safety concerns. Findings were meticulously recorded to facilitate a thorough understanding of astaxanthin's therapeutic implications.

Synthesis of results

The synthesis of results involved a detailed analysis of the extracted data from the selected studies. This aimed to clarify astaxanthin's mechanisms of action in KOA, its overall efficacy, and its safety profile. The synthesis also identified future research directions, highlighting gaps in the literature and suggesting areas for further investigation. This comprehensive approach provided valuable insights into astaxanthin's role in managing knee osteoarthritis and potential clinical applications.

Results

Antioxidant activity of astaxanthin

KOA, a condition that affects the joints, oxidative stress is a major problem. An excess of harmful molecules causes this stress called reactive oxygen species (ROS).[6] These ROS damage the tendon in the joints and increase inflammation, making the condition worse over time. Astaxanthin is a powerful antioxidant that can help protect the joints from this damage. Antioxidants are substances that neutralize reactive oxygen species, preventing them from harming cells. When ROS levels get too high, they disrupt the balance between harmful molecules and the body's natural defenses.[6] This is where astaxanthin comes in: it efficiently neutralizes these harmful molecules, stopping them from damaging the cartilage. Astaxanthin does more than just neutralize ROS. It also prevents lipid peroxidation, a process where ROS damage the fats in cell membranes.[7] This damage can lead to further inflammation and instability in the cells. By stopping lipid peroxidation, astaxanthin helps continue the integrity of cell membranes, reducing inflammation and protecting the joints.[7] Moreover, astaxanthin enhances the activity of crucial enzymes like superoxide dismutase (SOD) and catalase.[8] These enzymes play a key role in defending against oxidative stress. SOD converts superoxide radicals, a type of ROS, into less harmful molecules, while catalase breaks down hydrogen peroxide, another harmful molecule, into water and oxygen. By boosting the activity of these enzymes, astaxanthin strengthens the body's natural defenses against oxidative stress, further protecting the cartilage in the joints from injury.[8]

Anti-inflammatory properties of astaxanthin

In the painful world of arthritis, where inflammation causes significant damage to the joints, astaxanthin acts like a calming force, reducing this inflammation effectively.[9] Inflammation in the joints is controlled by complex signaling pathways, much like a complicated web. Astaxanthin phases in and skillfully manages these pathways, especially the important ones like nuclear factor kappa B (NF-κB) and mitogen-activated protein kinase (MAPK).[9] These pathways are accountable for producing substances that cause inflammation. When NF-κB is activated, it triggers a chain reaction that leads to increased inflammation. Astaxanthin helps by stopping NF-κB from being activated, which in turn reduces the production of inflammatory substances.[10] Similarly, it affects the MAPK pathways, preventing the chain of events that would normally lead to more inflammation. By

controlling these pathways, astaxanthin reduces the levels of pro-inflammatory cytokines like interleukin-1 beta (IL-1β) and also tumor necrosis factor-alpha (TNF-α), which are main contributors to pain and stiffness in arthritis.[11] As the levels of these cytokines decrease, so does the pain and also stiffness in the joints. This makes astaxanthin a valuable aid in providing relief from the symptoms of arthritis and also in managing the disease.[12]

Cartilage protection mechanism by astaxanthin

In the delicate balance of joint health, preserving the integrity of cartilage is crucial for slowing the progression KOA.[13] Picture astaxanthin as a vigilant guardian of this precious cartilage, armed with the ability to protect it from the forces that seek to degrade it.[13] This powerful antioxidant does more than just defend; it actively supports the regeneration of cartilage by stimulating the production of essential components like collagen and proteoglycans.[14] These components are vital, as they provide the cartilage with the strength and resilience it needs to endure the constant pressure and movement of the joints.[14] Astaxanthin's protective reach extends to combating matrix metalloproteinases (MMPs), enzymes that play a significant role in the breakdown of cartilage. MMPs can be thought of as destructive architects, chiseling away at the cartilage and weakening its structure. By inhibiting the activity of these enzymes, astaxanthin prevents this relentless destruction, helping to maintain the cartilage's integrity and function.[15] The multifaceted benefits of astaxanthin in KOA management are remarkable. It acts as an antioxidant, neutralizing harmful molecules that contribute to oxidative stress. It also has anti-inflammatory properties, reducing the inflammation that causes pain and swelling in the joints.[15] Furthermore, by protecting and regenerating cartilage, astaxanthin addresses one of the root causes of KOA, offering more than just symptomatic relief. Astaxanthin stands out as a beacon of hope for those suffering from KOA. Its ability to reduce pain and inflammation while also preserving joint function makes it a powerful ally in the fight against this debilitating condition.[15] However, the full extent of astaxanthin's capabilities is still being uncovered. Researchers are continually exploring its mechanisms to better understand how it can be used to its fullest potential.[16] As science delves deeper into the benefits of astaxanthin, there is hope that it will lead to even more effective treatments for those afflicted by knee osteoarthritis, offering not just relief but a chance at better joint health and improved quality of life.[16] These detailed mechanisms underscore the multifaceted therapeutic potential of astaxanthin in KOA management. By targeting oxidative stress, inflammation, and cartilage degradation, astaxanthin offers a promising approach for alleviating symptoms and slowing disease progression in KOA (See Table 1 for summary of the mechanism of action of astaxanthin).

Table 1 Summary of astaxanthin's mechanisms of action in knee osteoarthritis

Mechanism description	References
Antioxidant activity	
Astaxanthin scavenges ROS, inhibits lipid peroxidation, and enhances the activity of endogenous antioxidant enzymes like SOD and catalase.	7, 8, 9
Anti-inflammatory	
Astaxanthin modulates NF-κB and MAPK signaling pathways, leading to downregulation of pro-inflammatory cytokines such as IL-1β and TNF-α.	10, 11, 12
Cartilage protection	
Astaxanthin promotes cartilage matrix synthesis, inhibits MMP activity, and preserves cartilage integrity, thereby mitigating disease progression in knee osteoarthritis.	13, 14

ROS, reactive oxygen species; SOD, superoxide dismutase

Therapeutic effect of astaxanthin

Preclinical evidence of astaxanthin

Preclinical studies have played a key role in revealing the potential benefits of astaxanthin for treating KOA.[17] By using a variety of animal models that closely mimic the complex characteristics of KOA in humans, researchers have been able to investigate how astaxanthin affects various aspects of the disease.[17] These studies have shown that astaxanthin can reduce pain and inflammation, protect against cartilage degradation, and improve overall joint health. Through these detailed investigations, researchers have gained valuable insights into the mechanisms by which astaxanthin works, providing strong evidence of its therapeutic potential in managing KOA.[18] In the realm of preclinical exploration, a rich tapestry of animal models serves as the canvas upon which the effects of astaxanthin unfold. From surgically induced models, such as the destabilization of the medial meniscus (DMM) in rodents, to chemically induced models like the monosodium iodoacetate (MIA) injection model, each animal model offers unique insights into astaxanthin's therapeutic potential.[19] Additionally, non-traditional models, including genetically modified mice with cartilage-specific alterations, further enrich the narrative, providing a nuanced understanding of astaxanthin's effects across diverse disease phenotypes.[20]

The narrative of preclinical studies resonates with a symphony of findings, each chord a testament to astaxanthin's transformative potential in KOA management.[21] Histological examinations unveil a landscape adorned with signs of healing, as astaxanthin supplementation attenuates cartilage degradation, suppresses synovial inflammation, and mitigates osteophyte formation.[21] Beyond the realm of histology, functional assessments illuminate the path to restoration, with astaxanthin offering respite from the shackles of pain and dysfunction.[21] Moreover, mechanistic insights gleaned from these studies unveil a tapestry of molecular interactions, as astaxanthin's antioxidative and anti-inflammatory virtues emerge as guiding beacons in the realm of joint homeostasis[22] (See Table 2 for summary).

Clinical evidence of astaxanthin

As the curtain rises on the realm of clinical inquiry, the narrative of astaxanthin's therapeutic potential unfolds, offering a beacon of hope amidst the shadows of disease. Within the realm of clinical inquiry, a diverse array of study designs serves as a crucible for testing the waters of astaxanthin's efficacy in KOA

Table 2 Preclinical evidence of astaxanthin's therapeutic effects on knee osteoarthritis

Animal Model	Characteristics	Astaxanthin effects	References
Surgically induced models	Destabilization of the medial meniscus)	Attenuation of cartilage degradation suppression of synovial inflammation Mitigation of osteophyte formation	19, 20, 21, 22
Chemically induced models	Monosodium iodoacetate injection model	Reduction in pain and inflammation Protection against cartilage degradation Improvement in overall joint health	17, 18, 19, 20, 21, 22
Genetically modified mice	Cartilage-specific alterations	Insights into astaxanthin's effects across diverse disease phenotypes	20

management.[23] From randomized controlled trials meticulously crafted to elucidate causality to observational studies offering glimpses into real-world effectiveness, each study design contributes to the evolving narrative of astaxanthin's therapeutic potential. Moreover, meta-analyses serve as compasses, guiding the trajectory of evidence synthesis and informing clinical decision-making amidst the sea of uncertainty.[24] At the heart of clinical inquiry lie outcome measures, each offering a window into the realm of patient experience and disease progression.[25] From the subjective realms of pain assessment, as measured by visual analog scales and numeric rating scales, to the objective domains of joint function, as quantified by the Western Ontario and McMaster Universities Osteoarthritis Index, each measure serves as a touchstone for evaluating astaxanthin's impact on KOA-related symptoms and functional outcomes.[26] Within the annals of clinical inquiry, astaxanthin emerges as a harbinger of hope, offering respite from the burdens of disease and the promise of a brighter tomorrow.[26] Across diverse study populations and intervention regimens, astaxanthin supplementation consistently demonstrates significant improvements in pain relief, joint function, and quality of life among KOA patients.[26] Furthermore, biomarker analyses unveil a landscape adorned with signs of healing, as astaxanthin supplementation mitigates inflammatory markers and preserves cartilage integrity, offering a glimmer of hope amidst the shadows of disease progression.[27] As the saga of astaxanthin's therapeutic potential continues to unfold, each chapter offers a glimpse into the transformative power of this natural compound in the realm of KOA management. Yet, amidst the triumphs lie untrodden paths of exploration, beckoning researchers to delve deeper into the intricacies of astaxanthin's mechanisms and optimize its therapeutic potential for the betterment of those afflicted by knee osteoarthritis.[27] See Table 3 as a summary of clinical trials on astaxanthin for KOA.

Comparative analysis with existing treatments

Astaxanthin presents an auspicious alternative in the management of KOA when compared to conventional treatments like nonsteroidal anti-inflammatory drugs (NSAIDs) and corticosteroids.[23] While NSAIDs are widely used for their rapid relief from pain and inflammation, they often come with noteworthy long-term side effects, such as gastrointestinal issues, cardiovascular risks, and kidney damage. Corticosteroids, on the other hand, provide effective short-term relief but can lead to joint degradation and systemic complications when used frequently. In contrast, astaxanthin, a natural antioxidant, offers a safer profile with its potent anti-inflammatory and cartilage-protective effects, without the adverse effects typically associated with synthetic drugs.[19] As a therapeutic agent that addresses the root cause of inflammation, rather than just masking the symptoms, astaxanthin's ability to neutralize RO and inhibit key inflammatory pathways like NF-κB positions it. Unlike corticosteroids, which can accelerate cartilage breakdown over time, astaxanthin promotes cartilage regeneration by stimulating collagen production and inhibiting matrix metalloproteinases. This dual action of reducing inflammation and protecting cartilage makes astaxanthin not just a symptom-reliever, but a potential disease-modifying agent in KOA management.[28] Furthermore, while NSAIDs provide temporary relief, they do not halt the progression of osteoarthritis. Astaxanthin's antioxidative properties help in slowing the degradation process, potentially leading to better long-term joint health. Its natural origin also makes it a more appealing option for patients seeking alternatives to synthetic drugs with fewer side effects.[29] Thus, in the landscape of KOA treatment, astaxanthin stands out for its holistic approach to managing both the symptoms and underlying pathology of the disease, offering a safer and potentially more effective long-term solution compared to traditional treatments.

Safety profile and adverse effects of astaxanthin

In harnessing astaxanthin's therapeutic potential for KOA management, ensuring its safety profile is paramount.[30] Both preclinical and clinical investigations have shed light on the safety considerations surrounding astaxanthin supplementation, offering valuable insights into its tolerability and potential adverse effects. Preclinical studies serve as foundational pillars in the assessment of astaxanthin's safety profile, providing a preliminary glimpse into its tolerability and toxicity in animal models.[31] These studies have yielded reassuring findings, indicating that astaxanthin is usually well-tolerated at therapeutic dosages, with no significant toxic effects reported.[32] Animal models have exhibited minimal adverse effects following astaxanthin supplementation, further bolstering confidence in its safety for potential clinical use. Furthermore, long-term toxicity studies have failed to unveil any discernible adverse outcomes, reaffirming the benign nature of astaxanthin supplementation in animal subjects.[32]

Transitioning from the controlled confines of preclinical investigations to the dynamic landscape of clinical trials, the safety profile of astaxanthin

Table 3 Summary of clinical trials on astaxanthin for knee osteoarthritis

Study design	Sample size	Dosage and duration	Outcome measures	Key findings	References
Randomized controlled trial	100 patients	12 mg/day for 6 months	Pain scores, joint function, quality of life	Significant reduction in pain, improved joint function, and quality of life	23, 24
Double-blind, placebo-controlled trial	80 patients	8 mg/day for 3 months	Pain scores, inflammatory markers	Decreased pain and inflammatory markers compared to placebo	24
Open-label study	50 patients	16 mg/day for 12 weeks	Pain scores, cartilage thickness	Reduction in pain, preservation of cartilage thickness	25,26

continues to shine brightly. Clinical trials exploring the safety of astaxanthin supplementation in KOA patients have reported a paucity of adverse effects, underscoring its favorable tolerability profile.[33] Among the few adverse effects reported, mild gastrointestinal symptoms such as nausea and diarrhea feature prominently, albeit transient in nature and typically resolving with continued supplementation.[33] Furthermore, anecdotal reports of temporary changes in skin pigmentation have surfaced, although these effects are considered benign and reversible upon discontinuation of astaxanthin supplementation.[33] Overall, clinical studies have painted a reassuring picture of astaxanthin's safety, suggesting that it is well-tolerated by most individuals, even at relatively high doses.[34]

While astaxanthin's safety profile appears commendable, prudent consideration of potential interactions and contraindications is warranted. Astaxanthin's purported antiplatelet effects raise concerns regarding potential interactions with certain medications, particularly anticoagulants and antiplatelet agents.[35] As such, individuals concurrently using these medications should exercise caution and seek guidance from healthcare professionals before embarking on astaxanthin supplementation. Moreover, individuals with known allergies to astaxanthin or related compounds should approach supplementation with caution to mitigate the risk of allergic reactions. While astaxanthin holds promise as a safe and efficacious therapeutic adjunct for KOA management, judicious evaluation of individual medical histories and medication regimens is imperative to ensure optimal safety and efficacy outcomes. Preclinical and clinical studies have shown that astaxanthin is generally well-tolerated, with minimal adverse effects such as mild gastrointestinal symptoms and temporary skin pigmentation changes.[36] However, individuals on anticoagulant medications or those with specific allergies should consult healthcare professionals before using astaxanthin to avoid potential interactions and ensure safety (see Table 4 for a summary).

Table 4 Safety profile of astaxanthin supplementation in knee osteoarthritis

Adverse Effects	Frequency	Severity	Management	References
Gastrointestinal symptoms (e.g., nausea, diarrhea)	Common	Mild	Usually transient; resolves with continued supplementation	28,29
Skin pigmentation changes	Rare	Gentle	Reversible upon discontinuation of supplementation	32,33
Allergic reactions	Rare	Variable	Avoid supplementation in individuals with known allergies	30,36

Future research directions and research gaps

As the horizon of astaxanthin research expands, navigating the uncharted territories of future investigations holds the promise of unlocking new frontiers in KOA management.[36] Within this landscape, several critical avenues beckon researchers to delve deeper, bridging existing knowledge gaps and charting a course toward enhanced clinical efficacy and patient outcomes. The journey to perfecting astaxanthin therapy for KOA hinges on discovering the optimal dosing regimens. This quest is akin to solving a complex puzzle, where each piece represents a different aspect of treatment. Researchers are on a mission to understand how various doses of astaxanthin interact with different patient characteristics, such as age, the severity of the disease, and the length of treatment.[37] Imagine this process as a detailed exploration. Scientists need to map out the relationships between dose and response, meticulously examining how astaxanthin works in diverse scenarios. They aim to uncover the ideal amounts and frequencies of administration that offer the best therapeutic results while minimizing any potential side effects. Consider a patient with KOA—perhaps an elderly person with advanced disease or a younger individual in the early stages. Each of these patients might require a different approach to astaxanthin therapy. By conducting thorough research and trials, scientists can determine the specific dosing thresholds that are most effective for each type of patient. This way, they can craft personalized treatment plans that cater to individual needs, much like a tailor customizes a suit to fit perfectly.[38] The ultimate goal of this research is to create a roadmap for astaxanthin dosing that doctors can follow, ensuring that each patient receives a treatment plan that is both safe and highly effective. This personalized approach promises not only to alleviate symptoms more efficiently but also to enhance the overall quality of life for that battling knee osteoarthritis. Through dedicated research and careful consideration of various patient factors, the future of astaxanthin therapy looks bright, offering hope for a more precise and effective management of KOA.[38]

While we've seen some promising glimpses of astaxanthin's potential benefits in short-term clinical trials, there's a vast horizon of inquiry awaiting exploration, particularly concerning its long-term effects and potential for modifying the progression of KOA. To truly understand the impact of astaxanthin over time, researchers are calling for prospective longitudinal studies that track patients for extended durations. These studies would help ascertain whether astaxanthin supplementation can sustainably halt the progression of KOA and maintain the integrity of the joints.[38] Researchers carefully observe how astaxanthin affects patients' health over time. By scrutinizing structural outcomes such as changes in cartilage thickness and narrowing of the joint space, scientists aim to uncover whether astaxanthin has the potential to change the natural course of KOA. This isn't just about relieving symptoms; it's about finding

Table 5 Future research directions for astaxanthin in knee osteoarthritis (KOA)

Research direction	Description
Optimization of dosing regimens	Explore dose-response relationships and optimal treatment durations to establish effective and sustainable dosing strategies for long-term KOA management.
Exploration of long-term effects and disease modification	Conduct longitudinal studies to assess the sustained efficacy of astaxanthin in modifying disease progression, joint integrity, and structural outcomes in KOA patients over extended treatment periods.
Investigation of combination therapies	Investigate synergistic effects of astaxanthin with conventional therapies and natural compounds in combination therapy approaches to enhance treatment outcomes and address multiple pathophysiological pathways in KOA.
Exploration of mechanistic insights	Utilize advanced molecular techniques to elucidate the molecular pathways modulated by astaxanthin in KOA, providing deeper mechanistic insights and identifying potential therapeutic targets.
Assessment of patient stratification and personalized medicine	Investigate patient stratification strategies based on clinical characteristics, biomarkers, and genetic profiles to personalize astaxanthin supplementation in KOA management and optimize treatment outcomes through personalized medicine approaches.

treatments that could fundamentally alter the trajectory of the disease itself. Instead of just managing symptoms, they could have access to therapies that slow down or even stop the progression of the disease, preserving joint function and quality of life for years to come. It's a vision of hope—an aspiration for disease-modifying interventions that could revolutionize the way we approach osteoarthritic degeneration. But to reach this goal, we need dedicated research—studies that delve deep into the long-term effects of astaxanthin and its potential to transform the lives of KOA patients. These studies hold the promise of unlocking new avenues of treatment, offering a glimmer of hope in the ongoing battle against osteoarthritis.[38]

The potential synergy between astaxanthin and conventional therapies in managing KOA opens up a rich landscape for further investigation. Researchers are eager to delve into the realm of combination therapies, where astaxanthin could be paired with established treatments like NSAIDs, pain relievers, and physical therapy. By studying how these treatments work together, scientists hope to uncover new ways to improve outcomes for KOA patients. But the exploration doesn't stop there.[39] Researchers also want to explore multimodal approaches, which involve combining astaxanthin with other natural compounds that have complementary effects. These compounds might have different ways of targeting the symptoms and causes of KOA, and when combined with astaxanthin, they could enhance treatment efficacy while reducing side effects. By combining the strengths of traditional treatments with the potential of astaxanthin and other natural compounds, they aim to create a more holistic approach to care. This integrative approach could offer patients a wider range of treatment options and ultimately lead to better outcomes and improved quality of life for those living with KOA. Beyond its promising therapeutic potential, astaxanthin holds secrets within its molecular structure that scientists are eager to uncover. Imagine diving into a mysterious labyrinth beneath the surface, where each pathway leads to a deeper understanding of how astaxanthin works. In the future, researchers plan to embark on a journey of discovery, using advanced molecular techniques like transcriptomics, proteomics, and metabolomics to decode the intricate mechanisms behind astaxanthin's effects in KOA. This exploration as a scientific endeavor, where researchers employ sophisticated tools to elucidate the intricate molecular pathways traversed by astaxanthin within the body. As they unravel these molecular mysteries, they hope to find new targets for treatment—like unlocking secret doors in a maze, revealing pathways to better care for KOA patients. This journey into the molecular world of astaxanthin isn't just about understanding how it works; it's about opening doors to precision medicine, where treatments are tailored to each individual's unique needs.[40]

In the era of precision medicine, the quest for tailored therapeutic strategies represents a beacon of hope in optimizing treatment outcomes for KOA.[26] Looking ahead, future research endeavors are poised to embark on a multifaceted journey of patient stratification. This intricate process involves the integration of diverse parameters, including clinical phenotypes, biomarkers, and genetic profiles, to categorize individuals into distinct subgroups. By adopting such a multidimensional approach, researchers aim to gain deeper insights into the heterogeneous nature of KOA and its varied treatment responses across different patient cohorts. This endeavor holds promise for unraveling the underlying mechanisms driving divergent disease trajectories and treatment outcomes. Moreover, it presents an opportunity to identify prognostic biomarkers that serve as reliable indicators of both treatment efficacy and disease progression.[41] Through meticulous patient stratification, researchers envision a paradigm

shift towards personalized medicine in KOA management. By tailoring astaxanthin supplementation to the unique profiles of individual patients, clinicians can optimize treatment efficacy while minimizing the risk of adverse effects.[42] This personalized approach not only enhances therapeutic precision but also fosters a more patient-centric model of care, wherein interventions are finely tuned to address the specific needs and characteristics of each individual. In essence, the pursuit of tailored therapeutic approaches in KOA heralds a new era of precision medicine, wherein the convergence of clinical insights, molecular biomarkers, and genetic profiling empowers clinicians to deliver customized care that is both effective and personalized.[43] Future research in astaxanthin therapy for KOA should focus on optimizing dosing regimens, exploring long-term effects, investigating combination therapies, delving into mechanistic insights, and assessing patient stratification for personalized medicine.[44] By addressing these research gaps, it can be paved the way for more effective, personalized treatments that improve outcomes and quality of life for KOA patients, marking a significant stride towards precision medicine in KOA management (see Table 5 for summary). These future research directions aim to address key knowledge gaps and advance our understanding of astaxanthin's role in knee osteoarthritis management, paving the way for improved treatment strategies and better outcomes for affected individuals.

Discussion

Astaxanthin has gathered significant attention as a therapeutic candidate for KOA, given its unique ability to address multiple aspects of the disease's pathophysiology. This review emphasizes the compound's antioxidative, anti-inflammatory, and also cartilage-protective mechanisms, which composed offer a comprehensive approach to managing KOA. By neutralizing oxidative stress, a known driver of cartilage degradation, and inhibiting pathways responsible for inflammation, astaxanthin not only alleviates symptoms but also shows potential for varying disease progression. Moreover, its role in promoting cartilage synthesis positions it as more than a symptomatic treatment, setting it apart from conventional opportunities. When compared to usually used therapies such as NSAIDs and corticosteroids, astaxanthin presents distinct advantages. These conventional treatments often target immediate symptom relief, yet their long-term use is flawed by side effects including gastrointestinal issues and also accelerated cartilage breakdown. Astaxanthin's natural origin and also minimal side effect profile make it a practical alternative or adjunct, especially for patients looking for sustainable and holistic options. While the findings are promising, several research gaps must be talked to fully harness astaxanthin's potential. Current studies are limited in duration, leaving questions about its long-term efficacy and also safety unanswered. Additionally, inconsistencies in dosing protocols across studies complicate the growth of standardized treatment guidelines. The potential for synergistic effects when shared with other therapies remains largely unexplored, representing a missed opportunity to improve treatment outcomes. Lastly, the lack of stratified studies considering patient-specific factors, such as age or genetic predisposition, underscores the need for personalized approaches to maximize efficacy. The combination of astaxanthin into clinical practice could mark a paradigm shift in KOA management. Future research must aim to fill these gaps by conducting long-term, well-designed studies that explore optimal dosing, combination therapies, and also personalized treatment strategies. This would not only solidify astaxanthin's position as a therapeutic option but also improve outcomes for patients living with this incapacitating condition.

Limitations

This review is limited by its reliance on published data, which may introduce bias due to the selective reporting of positive outcomes. Additionally, including studies with diverse methodologies and varying quality poses challenges to drawing definitive conclusions. Future reviews should incorporate more standardized and comprehensive criteria to address these limitations.

Conclusion

Astaxanthin presents a compelling prospect as a therapeutic intervention for KOA, due to its potent antioxidative and anti-inflammatory properties. Future research endeavors should prioritize refining dosing strategies, elucidating long-term effects, and also uncovering the underlying mechanisms of astaxanthin's action in KOA management. Such investigations hold the potential to inform the development of personalized treatment modalities personalized to the individual needs of KOA patients, thereby enhancing clinical outcomes and quality of life. Astaxanthin's auspicious safety profile, coupled with its demonstrated efficacy in preclinical and clinical studies, underscores its role as a promising adjunctive therapy in the comprehensive management of KOA.

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Conception or design of the work; or the acquisition, analysis, or interpretation of data for the work: AHMMR. *Drafting the work or reviewing it critically for important intellectual content:* AHMMR, SS, AHB. *Final approval of the version to be published:* AHMMR, SS. *Accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved:* AHMMR, SS, AHB.

Conflict of interest

We do not have any conflict of interest.

Data availability statement

We confirm that the data supporting the findings of the study will be shared upon reasonable request.

Supplementary file

None

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