Review

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Review

The Pharmaceutical Potential of α- and β-Amyrins

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Abstract: (1) Plant-derived pharmaceuticals represent a highly compelling area of research and continue to attract significant interest from countries, regions, scientific communities, and pharmaceutical companies worldwide. Among these, α- and β-amyrins have been identified as high-value triterpenoid compounds with a broad spectrum of potential therapeutic properties, including anti-inflammatory, anti-diabetic, anti-atherosclerotic, analgesic, anti-gout, neuroprotective, anti-Parkinsonian, anticancer, antibacterial, and anti-HIV activities (2) Methods: Relevant information and data were obtained through comprehensive searches of major scientific databases, including Web of Science, Elsevier, and the National Library of Medicine (3) Results: This study highlighted the pharmaceutical potential of α- and β-amyrins, supported by specific evidence from in vivo, in vitro, and clinical trials. Various extraction methods for α- and β-amyrins have been discussed, followed by recommendations for future directions in the development of these compounds as pharmaceutical agents and functional food ingredients (4) Conclusions: This document served as a vital reference for harnessing the therapeutic potential of α- and β-amyrin compounds in the prevention and treatment of various serious diseases worldwide, potentially opening new opportunities and directions for the pharmaceutical industry.

Keywords: α- and β-Amyrins; Anti-inflammatory; Anti-diabetes; Anti-atherosclerosis; Antinociceptive; Anti-gout; Positive Effects on Nerves; Anti-Parkinsonian; Anticancer; Antibacterial; Anti-HIV

1. Introduction

Pharmaceuticals play a crucial and indispensable role in global healthcare. Nowadays, they are no longer viewed merely as commercial commodities but are recognized as essential necessities for maintaining and improving human health [1]. Pharmaceuticals remain a fundamental component in the prevention and treatment of diseases, as well as in the promotion of overall public health [2]. Pharmaceuticals are widely recognized as a socially significant commodity, directly impacting human health and well-being. Therefore, ensuring quality, safety, and efficacy is essential [3]. Pharmaceuticals are essential for the treatment and prevention of diseases, as well as for improving users' physical health [4]. Pharmaceuticals have contributed to extending and enhancing the lives of billions of people worldwide [5]. The global demand for pharmaceuticals is increasing rapidly,

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necessitating the expansion and advancement of production capabilities [6]. The global pharmaceutical market was valued at approximately USD 230.03 billion in 2021 and is expected to reach USD 430.05 billion by 2028, reflecting a compound annual growth rate (CAGR) of 11.32% [7]. The rapidly growing global population, coupled with escalating environmental pollution, has contributed to the rising demand for pharmaceuticals and significantly impacts worldwide pharmaceutical consumption [8]. In recent decades, the research and development of pharmaceuticals has received significant attention from governments, scientists, companies, individuals, and organizations in the world [9]. In global standards for evaluating living conditions, ensuring access to medicine for healthcare is considered a vital benchmark. This is why world leaders consistently prioritize the development of pharmaceuticals as a key component of social security and national development [10]. Following the Covid-19 pandemic and the predictions of future natural disasters that may lead to the emergence of new diseases, the position and role of the pharmaceutical industry have become more critical than ever. As a result, this field is increasingly attracting scientific research aimed at analyzing viral variants and pathogens to develop effective strategies for combating more dangerous and complex diseases [11]. If the position of the pharmaceutical industry is destabilized, it could lead to shortages of essential medicines, resulting in widespread anxiety and disruption within society, potentially even impacting socio-political stability [12]. Additionally, in the context of rapid population growth, ongoing conflicts, and the emergence of epidemics, the demand for medicines continues to rise, further complicating the global healthcare landscape [13]. The global trend increasingly focuses on using natural products like raw materials to produce medicines, health supplements, cosmetics, functional foods, nutritional products, and herbal beverages, all aimed at promoting and protecting human health [14]. Triterpenoids are a group of naturally occurring chemical compounds found in various animal and plant species [15,16]. Triterpenoids play diverse roles in chemistry, serving as precursors for the synthesis of various compounds, including steroids and saponins [17]. Triterpenoids are regarded as key components in traditional medicine across many countries, including China, Japan, Korea, and Vietnam [18]. Triterpenoids are compounds found in numerous plants, belonging to the isoprenoid group. These compounds are often present in plants as glycosides and saponins. Due to their diverse bioactivities and abundant availability, triterpenoids are considered a promising source of raw materials for the pharmaceutical industry [19]. α-Amyrin and β-amyrin are two representative compounds within the triterpenoid group [20]. α-Amyrin (with an ursane skeleton) and β-amyrin (with an oleanane skeleton) are two typical compounds with similar chemical structures, both classified within the triterpene acid group [21]. Among these, ursane-type triterpenes, derived from α-amyrin, are the most common triterpenes, while oleanane-type triterpenes are produced from β-amyrin [22]. These two compounds have been extensively researched and successfully extracted by the author in significant quantities (10.75 g/kg) from the leaves of *Celastrus hindsii* [23]. This study demonstrates the potential medicinal value of α- and β-amyrins. It serves as a comprehensive summary of the value of these compounds, aiming to maximize the inherent potential of this mixture. The research has opened new opportunities for the development of the pharmaceutical industry.

2. Materials and Methods

This article synthesizes knowledge from leading, reputable sources worldwide. The information and data systems explored include SCI (Science Citation Index), SCIE (Science Citation Index Expanded), and ISI (Institute for Scientific Information), which encompasses high-quality scientific research across hundreds of thousands of journals globally. The research is based on a carefully selected database of 201 scientific articles from renowned publishers such as Springer, Elsevier, Wiley-Blackwell, Taylor & Francis, Oxford University Press, Cambridge University Press, University of Chicago Press, Inder Science Publishing, and Edward Elgar Publishing, ensuring accuracy from 2000 to 2025. Additionally, this study has been written by the author's own knowledge and experience, which have been consolidated in two research works published in the MDPI journal.

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3. Results

3.1. Anti-Inflammatory Potential of α- and β-Amyrins

The anti-inflammatory effects of α- and β-amyrins were evaluated in a rat model of acute periodontitis. In this study, periodontitis was induced by placing a ligature around the upper right second molar. Two hours prior to ligature placement, rats received intraperitoneal injections of α- and β-amyrins at doses of 5 - 10 mg/kg. Lumiracoxib and dexamethasone were used as positive controls, while a placebo group served as a negative control. Six hours after induction, plasma levels of tumor necrosis factor-α (TNF-α) were measured. After 24 hours, the rats were sacrificed, and gingival tissues were analyzed using myeloperoxidase activity and Thio barbituric acid reactive substances (TBARS) assays. The results showed that α- and β-amyrins, particularly at the 5 mg/kg dose, significantly reduced markers of inflammation. While lumiracoxib also produced variable effects on the measured parameters, α- and β-amyrins demonstrated notable efficacy in delaying acute inflammation. These findings support the potential of α- and β-amyrins as therapeutic agents for managing inflammation in periodontal disease and warrant further investigation into their role in preventing chronic bone loss [24].

Table 1. The Anti-inflammatory Activities of α- and β-Amyrins.

Disease	Cell Line (Receptors)	Duration	Doses of α- and β-Amyrins	Assay	References
Periodontal	TNF-α	24 hours	5 - 10 mg/kg	Vivo	[24]
Persistent Inflammatory and neuropathic hyperalgesia	CB1, CB2	12 hours	30 mg/kg	Vivo	[25]
Colitis	COX-2, VEGF, NF-κB	72 hours	3 mg/kg	Vivo	[26]
Colitis	ICAM-1, VCAM-1, PCAM-1, β2-integrin, CD68, and P-selectin	0-7 days	1, 3 and 10 mg/kg	Vivo	[27]
Acute pancreatitis	(TNF-α), (IL-6)	24 hours	10, 30 and 100 mg/kg	Vivo	[28]

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The anti-inflammatory and analgesic potential of α- and β-amyrin was evaluated using models activated through cannabinoid receptor type 1 (CB1) and type 2 (CB2) pathways. The study showed that both compounds significantly reduced the production of pro-inflammatory cytokines and suppressed the expression of nuclear factor-kappa B (NF-κB) binding protein and cyclooxygenase (COX) enzymes. These findings suggest that α- and β-amyrins exert their anti-inflammatory effects, at least in part, by modulating the endocannabinoid system, underscoring their potential as therapeutic agents for treating inflammatory and pain-related disorders [25].

The anti-inflammatory activity of α- and β-amyrin was assessed using a murine model of colitis, with the compounds administered in a 1:1 mixture. Colitis was induced by rectal administration of trinitrobenzene sulphonic acid (TNBS), and mice were monitored over a 72-hours period. Systemic treatment with α- and β-amyrin (3 mg/kg, intraperitoneally) was compared to dexamethasone and vehicle-treated control groups. Disease progression was evaluated through macroscopic and microscopic assessment of colonic lesions, myeloperoxidase (MPO) activity, and cytokine levels. Immunohistochemical analysis was used to examine the expression of cyclooxygenase-2 (COX-2), vascular endothelial growth factor (VEGF), phosphorylated NF-κB (phospho-p65), and

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phosphorylated cyclic AMP response element-binding protein (phospho-CREB). TNBS-induced colitis was characterized by severe tissue damage, neutrophil infiltration, and elevated pro-inflammatory mediator levels. Treatment with α- and β-amyrin led to notable improvements in colonic tissue morphology, a significant reduction in polymorphonuclear cell infiltration, decreased levels of interleukin-1β (IL-1β), and restoration of anti-inflammatory interleukin-10 (IL-10) in the colon. Moreover, α- and β-amyrin significantly downregulated VEGF expression and inhibited the expression of COX-2, phospho-NF-κB, and phospho-CREB. These findings demonstrate that α- and β-amyrin possess strong anti-inflammatory properties in TNBS-induced colitis and support their potential as therapeutic agents for managing inflammatory bowel diseases [26].

α- and β-Amyrin have demonstrated significant anti-inflammatory properties, particularly through modulation of the endocannabinoid system. In a murine model of dextran sulfate sodium (DSS)-induced colitis, treatment with α- and β-amyrin markedly reduced the severity of colonic lesions. This therapeutic effect was associated with decreased activity of inflammatory enzymes, including myeloperoxidase (MPO) and N-acetyl glucosamines. Administration of the triterpenes also significantly reduced levels of pro-inflammatory cytokines such as tumor necrosis factor-alpha (TNF-α), interleukin-1β (IL-1β), and various chemokines, while enhancing the expression of the anti-inflammatory cytokine interleukin-4 (IL-4). Moreover, α- and β-amyrin downregulated mRNA expression of several adhesion molecules involved in leukocyte recruitment and inflammation, including intercellular adhesion molecule-1 (ICAM-1), vascular cell adhesion molecule-1 (VCAM-1), platelet cell adhesion molecule-1 (PCAM-1), β2-integrin, CD68, and P-selectin. Importantly, the compounds also inhibited cannabinoid receptor type 1 (CB1), suggesting their role in modulating cannabinoid-mediated signaling. Additionally, they suppressed the expression of endocannabinoid-degrading enzymes such as monoglyceride lipase (MGL1) and fatty acid amid hydrolase (FAAH), thereby enhancing endocannabinoid tone. Collectively, these findings support the therapeutic potential of α- and β-amyrin as novel agents for the treatment of inflammatory diseases, particularly those involving cannabinoid system dysregulation [27].

α- and β-Amyrin have demonstrated considerable therapeutic potential in the treatment of acute pancreatitis. In a model of pancreatitis induced by L-arginine, treatment with these triterpenes significantly reduced the elevated wet weight/body weight ratio of the pancreas an established marker of inflammation and edema. Furthermore, α- and β-amyrin administration led to substantial decreases in serum amylase and lipase levels, key biochemical indicators of pancreatic injury. The compounds also markedly lowered concentrations of pro-inflammatory cytokines, including tumor necrosis factor-alpha (TNF-α) and interleukin-6 (IL-6). In pancreatic tissues, treatment with α- and β-amyrin reduced the activity of inflammation and oxidative stress markers such as myeloperoxidase (MPO), thiobarbituric acid reactive substances (TBARS), and nitrate/nitrite levels. Immunohistochemical analysis further confirmed reduced expression of TNF-α and inducible nitric oxide synthase (iNOS), reinforcing the anti-inflammatory effects observed. Collectively, these findings indicate that α- and β-amyrin exert both antioxidant and anti-inflammatory actions, highlighting their promise as potential therapeutic agents for the management of acute pancreatitis [28].

3.2. Anti-Diabetes Potential of α- and β-Amyrins

α- and β-Amyrins have demonstrated significant antidiabetic and hypolipidemic properties in experimental models. Oral administration of these compounds resulted in a marked reduction in blood glucose levels, total cholesterol, and serum triglycerides. At a dose of 100 mg/kg, α- and β-amyrin not only normalized blood glucose levels but also exhibited strong lipid-lowering effects. During oral glucose tolerance tests, elevated glucose concentrations were significantly reduced, indicating improved glucose metabolism. Additionally, plasma insulin levels and histopathological analysis of pancreatic tissue supported the beneficial role of α- and β-amyrin in preserving pancreatic function. Rats administered α- and β-amyrin at doses of 10, 30, and 100 mg/kg demonstrated a dose-dependent improvement in lipid profiles. Notably, treatment at 100 mg/kg led to a substantial decrease in very low-density lipoprotein (VLDL) and low-density lipoprotein (LDL) cholesterol

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levels, accompanied by an increase in high-density lipoprotein (HDL) cholesterol. These findings underscore the potential of α- and β-amyrin as therapeutic agents for managing hyperglycemia and dyslipidemia. Moreover, their efficacy in reducing risk factors associated with atherosclerosis suggests their promise as lead compounds in the development of novel treatments for diabetes and cardiovascular diseases [29].

β-Amyrin, extracted from the roots of *Hemidesmus indicus*, has demonstrated notable antidiabetic activity in experimental models. In particular, its derivative, β-amyrin palmitate, exhibited significant antihyperglycemic effects in glucose-loaded rats. Remarkably, this compound showed potent antidiabetic activity in both alloxan-induced and streptozotocin-induced diabetic rat models, even at a very low dose of 50 μg/kg body weight. The primary mechanism of action of β-amyrin palmitate appears to involve inhibition of intestinal glucose absorption, thereby reducing postprandial hyperglycemia. These results suggest that β-amyrin and its derivatives have strong potential as lead compounds for the development of future antidiabetic therapeutics [30].

β-Amyrin has been shown to possess significant antibacterial and antidiabetic properties through its enzymatic inhibitory activity. At a concentration of 24.24 μg/mL, β-amyrin effectively inhibited violacein production, with inhibition percentages ranging from 22.9 ± 1.2% to 42.1 ± 1.0%, suggesting its potential as an anti-quorum sensing agent. Furthermore, β-amyrin exhibited notable α-amylase inhibitory activity, achieving inhibition rates between 49.8 ± 0.3% and 69.3 ± 1.0% at a concentration of 10 μg/mL. In addition, β-glucosidase inhibition assays further confirmed the compound's effectiveness in targeting key carbohydrate-metabolizing enzymes. These findings highlight β-amyrin's dual functionality in both antimicrobial and antidiabetic roles, supporting its potential development as a multifunctional therapeutic agent [31].

α-Amyrin has demonstrated significant hypoglycemic activity in murine models and has been shown to exert dual effects on peroxisome proliferator-activated receptors (PPARδ and PPARγ) in 3T3-L1 adipocytes, highlighting its potential for the management of type 2 diabetes. Mechanistically, α-amyrin activates both PPARδ and PPARγ, along with adenosine monophosphate-activated protein kinase (AMPK) and protein kinase B (Akt). These signaling pathways are crucial for the translocation of glucose transporter 4 (GLUT4), which plays a pivotal role in enhancing insulin sensitivity and combating insulin resistance. Studies suggest that α-amyrin acts as an allosteric activator of AMPK, promoting GLUT4 translocation and improving glucose uptake in target tissues. Given these multiple mechanisms, α-amyrin is considered a promising bioactive molecule for the development of novel, multi-target therapeutic strategies aimed at addressing diabetes and its associated metabolic complications [32].

β-Amyrin has been identified as a promising antidiabetic compound with beneficial effects on preventing renal failure. In vivo, streptozotocin-induced diabetic rats were used as a model for diabetic nephropathy (DN), while in vitro, high glucose (HG)-stimulated human proximal tubular HK-2 cells served as an experimental model. β-Amyrin demonstrated its ability to alleviate renal injury in diabetic rats and reduce both the inflammatory response and apoptosis in HG-stimulated HK-2 cells. Mechanistically, β-amyrin induced the upregulation of miR-181b-5p, which was found to interact with high mobility group box 2 (HMGB2), as confirmed by luciferase reporter assays. Furthermore, β-amyrin promoted the downregulation of HMGB2 expression. Overexpression of HMGB2 was shown to reverse the protective effects of miR-181b-5p on the inflammatory response and apoptosis of HG-treated HK-2 cells, suggesting that β-amyrin exerts its renoprotective effects through the miR-181b-5p/HMGB2 axis. These findings underscore β-amyrin's potential as a therapeutic agent for managing diabetic nephropathy and preventing renal damage in diabetes [33].

β-Amyrin has demonstrated significant antidiabetic potential, as evidenced by its α-amylase inhibitory activity in vitro, with an IC_{50} of 19.50 μg, which is comparable to the standard antidiabetic drug acarbose (IC_{50}: 11.25 μg). Further computational studies revealed that β-amyrin exhibits high binding affinity to four key targets involved in diabetes regulation: glucagon-like peptide-1 (GLP-1), glycogen synthase kinase (GSK), glucokinase (GK), and insulin receptor tyrosine kinase (IRTK). Additionally, β-amyrin was found to possess favorable physicochemical properties, including high

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stability and bioactivity, a smaller energy gap, lower hardness, and higher softness, all of which contribute to its potential as a promising lead compound for antidiabetic drug development [34].

3.3. Anti-Atherosclerosis of α- and β-Amyrins

α- and β-Amyrins, isolated from a 95% ethanol extract of the fruits of the wild species *C. scabrifolia*, were evaluated for their lipid-lowering potential. Comprehensive spectroscopic and biochemical analyses were conducted to characterize the compounds. Their lipid-lowering activity was assessed using an in vitro HepG2 cell model. Results from molecular docking studies further supported the findings, indicating that both α- and β-amyrins exhibit strong potential as lipid-lowering agents [35].

α- and β-Amyrins were isolated from the stem and leaf extracts of *Rhus sylvestris* Siebold. Spectroscopic analysis confirmed the identity of the compounds, and cytotoxicity assays indicated that they were non-toxic at concentrations ranging from 0 to 1.0 μM. The compounds were further evaluated for their immunomodulatory properties, particularly their ability to inhibit cytokine secretion. In vitro studies using the murine macrophage cell line RAW264.7demonstrated that α- and β-amyrins significantly reduced lipopolysaccharide (LPS)-induced secretion of interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α). Notably, TNF-α secretion was inhibited even at a low concentration of 0.01 μM. These findings suggest that α- and β-amyrins hold promise as potential therapeutic agents for TNF-α-related inflammatory conditions, including transplant rejection, type II diabetes, and atherosclerosis [36].

α- and β-Amyrins, isolated from *Protium heptaphyllum*, have demonstrated significant anti-atherosclerotic potential and hepatoprotective effects. Using a mouse model of non-alcoholic fatty liver disease (NAFLD), male Swiss mice were fed a high-fat diet (HFD) for 15 weeks to induce fatty liver pathology. Histological analysis of liver tissue sections using hematoxylin and eosin (H&E) staining, along with biochemical evaluations, revealed that administration of α- and β-amyrins significantly attenuated hepatic steatosis and inflammation. Further mechanistic insights were obtained through RT-qPCR and western blotting, which showed that these compounds reversed the expression of key signaling pathways associated with lipid accumulation and inflammatory responses. These findings support the potential of α- and β-amyrins as therapeutic agents for the prevention and treatment of NAFLD [37].

α- and β-Amyrins, isolated from *Euphorbia hirta* L., have demonstrated potent anti-inflammatory effects, particularly in the context of vascular inflammation. In vitro assays were conducted using endothelial cells (SVEC4-10 cell line) treated with a medium composed of 50% lipopolysaccharide (LPS)-activated macrophage culture supernatant (RAW medium). Treatment with α- and β-amyrins significantly inhibited the expression of the endothelin-1 (ET-1) gene, a known pro-inflammatory and vasoconstrictive marker. Furthermore, α- and β-amyrins restored the mRNA expression of endothelial nitric oxide synthase (eNOS), which was otherwise suppressed by RAW medium exposure. These findings suggest that α- and β-amyrins may serve as effective therapeutic agents in the prevention of vascular disorders associated with chronic inflammation [38].

The effects of α- and β-amyrins on angiogenesis and the underlying molecular mechanisms were investigated using cultured human umbilical vein endothelial cells (HUVECs). Treatment with α- and β-amyrins was found to be non-cytotoxic to HUVECs. These compounds promoted angiogenic activity by enhancing tube-like structure formation and increasing cell migration. Moreover, α- and β-amyrins significantly stimulated the phosphorylation of Akt and endothelial nitric oxide synthase (eNOS), resulting in elevated nitric oxide (NO) production. These results suggest that α- and β-amyrins promote neovascularization in endothelial cells through an Akt-eNOS signaling-dependent mechanism. Therefore, α- and β-amyrins may represent promising therapeutic agents for the treatment of vascular diseases [39].

The effects of α- and β-amyrins (20 mg/kg for 15 days) on vascular reactivity were evaluated in a mouse model of diet-induced obesity. Mice were fed a high-fat diet (HFD) for 15 weeks to induce obesity. The contractile responses of isolated thoracic aorta to potassium chloride (KCl) and

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phenylephrine, as well as endothelium-dependent and -independent vasodilation induced by acetylcholine and sodium nitroprusside, respectively, were assessed. Treatment with α- and β-amyrins prevented HFD-induced vascular dysfunction by restoring the attenuated contractile response to phenylephrine and improving vasodilatory responses to both acetylcholine and sodium nitroprusside. Furthermore, α- and β-amyrin administration reversed impaired K^+ channel activation and restored the inhibitory effects of tetraethylammonium on vasodilation. These findings suggest that α- and β-amyrins exert significant vascular protective effects in the context of obesity-associated endothelial dysfunction [40].

3.4. The Antinociceptive Effect of α- and β-Amyrins

The analgesic activity of α- and β-amyrins, extracted from *Protium heptaphyllum*, was evaluated using a murine model of oral pain induced by formalin or capsaicin. Mice were administered α- and β-amyrin intraperitoneally at doses of 10, 30, and 100 mg/kg. Morphine (5 mg/kg, subcutaneously) and vehicle (3% Tween 80) served as controls. Pain was induced by injecting 20 μL of formalin (1.5%) or capsaicin (1.5 g) into the orofacial region. α- and β-Amyrins significantly reduced facial rubbing behavior in both pain models. Notably, at 30 mg/kg, α- and β-amyrins potentiated the second phase of the formalin response in a naloxone-sensitive manner, indicating involvement of peripheral opioid pathways. In the capsaicin-induced pain model, α- and β-amyrins exhibited a pronounced analgesic effect at the 100 mg/kg dose. These findings suggest that α- and β-amyrins exert antinociceptive effects through mechanisms at least partially mediated by peripheral opioid receptors [41].

The antinociceptive properties of α- and β-amyrins, extracted from *Protium kleinii*, were evaluated in rat models of visceral and inflammatory pain. Visceral pain was induced by intravenous injection of acetic acid, and the compounds were administered via both intraperitoneal and oral routes. The treatment provided rapid and effective pain relief. Further, α- and β-amyrins were assessed in central nervous system pain pathways through formalin injections into the hind paw, examining nociceptive responses at the level of the cerebral cortex and ventricles. The compounds effectively inhibited both the neurogenic and inflammatory phases of nociception. In addition, α- and β-amyrins reduced nociceptive responses induced by 8-bromo-cAMP (8-Br-cAMP), 12-O-tetradecanoylphorbol-13-acetate (TPA), and glutamate, indicating a broad analgesic profile. Notably, the antinociceptive effects appeared to be independent of classical opioid, α-adrenergic, serotoninergic, or nitrergic pathways. Furthermore, α- and β-amyrins significantly reduced mechanical hyperalgesia triggered by inflammatory mediators such as carrageenan, capsaicin, bradykinin, substance P, prostaglandin E2, 8-Br-cAMP, and TPA. These results suggest that α- and β-amyrins exert robust peripheral, spinal, and supraspinal antinociceptive effects, supporting their potential as novel agents for treating inflammatory and visceral pain [42].

The analgesic potential of α- and β-amyrins was demonstrated in the acetic acid-induced writhing test, where these compounds exhibited significant activity in reducing nociceptive responses. When administered orally, α- and β-amyrins effectively decreased the number of abdominal constrictions induced by acetic acid, indicating strong peripheral analgesic properties. Furthermore, in the formalin-induced pain model, α- and β-amyrins attenuated the behavioral responses associated with both the neurogenic and inflammatory phases of pain. These findings underscored the role of α- and β-amyrins in modulating pain perception and support their potential as therapeutic agents for the management of inflammatory and visceral pain [43].

Pharmacological activation of cannabinoid receptors CB1 and CB2 were a promising therapeutic strategy for the treatment of chronic pain and inflammation. In this context, α- and β-amyrins were investigated as bioactive compounds and demonstrated significant inhibition of persistent neuropathic pain and inflammation in murine models through oral administration. These triterpenes exerted their effects via both CB1 and CB2 receptor pathways. Notably, α- and β-amyrins exhibited strong inhibitory activity against the hydrolysis of 2-arachidonoyl glycerol (2-AG) in porcine brain homogenate, suggesting an indirect cannabimimetic mechanism. Rather than binding directly to cannabinoid receptors, α- and β-amyrins appear to enhance endocannabinoid signaling by

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preventing the enzymatic degradation of 2-AG. These findings position α- and β-amyrins as potential lead compounds for the development of novel analgesic and anti-inflammatory therapies targeting the endocannabinoid system [44].

3.5. Anti-Gout of α- and β-Amyrins

α- and β-Amyrin extracted from *Celastrus hindsii* were shown to possess anti-gout potential by inhibiting the activity of the xanthine oxidase (XO) enzyme, with an IC_{50} value of 258.22 μg/mL [23]. Compounds α- and β-amyrins, isolated from *Tabebuia roseoalba* leaves and identified in ethanol extracts by HPLC analysis, were shown to reduce serum uric acid concentrations and inhibit the inflammatory process associated with gout. The study evaluated their anti-hyperuricemic, hepatic xanthine oxidoreductase inhibitory, and anti-inflammatory activities in hyperuricemic rats and monosodium urate crystal-induced paw edema models. β-Amyrin significantly reduced serum uric acid levels in hyperuricemic rats by inhibiting hepatic xanthine oxidase activity and effectively reduced monosodium urate crystal-induced paw edema. These findings suggest that β-amyrin is a promising agent for the treatment of gouty arthritis, hyperuricemia, and related inflammatory conditions [45].

α- and β-Amyrin were isolated from the pericarp, heartwood, and seed of *Garcinia subelliptica*. Structural identification of these triterpenoids was confirmed through spectroscopic analysis, including techniques such as NMR and mass spectrometry. Both compounds demonstrated a notable inhibitory effect on xanthine oxidase (XO), an enzyme involved in purine metabolism and a key contributor to uric acid production. This suggests their potential anti-gout and antioxidant applications. Flow cytometric analysis revealed that treatment of NTUB1 cells with compound 1, either alone or in combination with cisplatin, resulted in cell cycle arrest and a significant increase in apoptotic cell death after 24 hours of exposure. These data suggested that the induction of cell cycle arrest and apoptosis in NTUB1 cells treated with compound 1 or with a combination of compound 1 and cisplatin for 24 hours is mediated by an increased production of reactive oxygen species (ROS) [47].

3.6. Positive Effects of α- and β-Amyrins on Nerves

α- and β-Amyrins were studied for their pharmacological effects on sleep in mice. The sleep was induced using pentobarbital, and the mice were then administered α- and β-amyrin at concentrations of 1, 3, or 10 mg/kg. The results showed that α- and β-amyrins significantly extended the sleep duration in mice. This suggests that α- and β-amyrins have potential anti-insomnia effects, likely through the activation of the GABAergic neurotransmitter system in the brain [48]. α- and β-Amyrins isolated from *Protium heptaphyllum* have demonstrated anticonvulsant, sedative, and anxiolytic properties. In the study, rats were treated with α- and β-amyrins at concentrations of 2.5, 5, 10, and 25 mg/kg (i.p. or orally). The results showed a significant increase in barbiturate-induced sleep duration, confirming the sedative effect. Additionally, the study found that tyrosine levels increased by 89%, while levels of GABA and glutamate decreased by 72%, 55%, and 60%, respectively. Furthermore, excitatory amino acids were reduced, and inhibitory amino acids were increased, suggesting a shift towards a more inhibitory neurotransmitter profile [49].

α- and β-Amyrins extracted from *Protium heptaphyllum* were evaluated for their ability to reduce capsaicin-induced analgesia in mice. The results demonstrated that orally administered α- and β-amyrins (doses ranging from 3 to 100 mg/kg) effectively inhibited pain sensation induced by capsaicin applied to the plantar (1.6 μg) and colon (149 μg). Notably, α- and β-amyrins did not alter sleep duration, nor did they impair walking, locomotion, or cause any observable abnormalities. Additionally, these compounds significantly blocked the hyperthermic response induced by capsaicin (10 mg/kg). These findings suggest that α- and β-amyrins may be potential compounds for analgesia, likely involving the vanilloid receptor (TRPV1) and opioid mechanisms [50].

The isolation of α- and β-amyrin from *Lobelia inflata* leaves was studied for its effects on the central nervous system in mice. The results showed that α- and β-amyrins significantly reduced the immobility time of mice in a dose-dependent manner (5, 10, and 20 mg/kg). These compounds also dose-dependently reduce locomotor activity and potentiated methamphetamine-induced locomotor

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antagonism. Unlike imipramine, α- and β-amyrins did not affect haloperidol-induced rigidity, tetrabenazine-induced ptosis, or apomorphine-induced stereotypy. They also had no effect on the 5-hydroxytryptophan-induced head-clonic reaction. Additionally, α- and β-amyrins (5, 10, and 20 mg/kg) had a stronger effect on pentobarbital sodium-induced delirium than imipramine (10, 20, and 40 mg/kg). These findings suggest that α- and β-amyrins exhibit sedative and antidepressant-like effects, comparable to the activity of meandering [51].

α- and β-Amyrin, components found in the waxy surface of tomatoes and dandelion coffee, have been shown to improve memory impairment caused by cholinergic dysfunction. These compounds act as PI3K inhibitors, which help reduce long-term potentiation (LTP) impairment. In studies on Aβ-injected mouse models of Alzheimer's disease, α- and β-amyrin were found to improve object recognition memory deficits. Furthermore, α- and β-amyrin treatment helped restore neurogenesis impairment induced by Aβ. These findings suggest that α- and β-amyrin are promising candidates for the treatment of Alzheimer's disease [52]. The isomer mixture of α- and β-amyrin found in the resin of *Protium heptaphyllum* has demonstrated potential as an anti-inflammatory agent. Additionally, these compounds have been shown to have a protective effect on both the central and peripheral nervous systems, helping the brain respond to various effects on the central nervous system [53].

3.7. Anti-Parkinsonian Effects of α- and β-Amyrins

α- and β-Amyrins have been shown to offer protective effects on dopaminergic neurons by reducing 6-hydroxydopamine (6-OHDA)-induced cell damage. These compounds exhibit strong antioxidant activity, reducing intracellular reactive oxygen species (ROS) in *C. elegans*. α- and β-Amyrins significantly decrease α-synuclein aggregation in the NL5901 transgenic strain, upregulate LGG-1 mRNA expression, and increase the number of localized LGG-1 dots in the DA2123 transgenic strain. These results suggest that α- and β-amyrins could be beneficial in the treatment and slowing of Parkinson's disease progression [54]. The use of α- and β-amyrins has been explored as a potential treatment to prevent Parkinson's disease by targeting misfolded proteins and damaged organelles. These effects have been tested through mechanisms related to LGG-1, suggesting that α- and β-amyrins may play a role in mitigating the underlying causes of Parkinson's disease [55]. Autophagy has been recognized as a promising therapeutic approach for preventing Parkinson's disease, as it plays a crucial role in eliminating misfolded proteins and damaged organelles, which are key contributors to the disease's progression [56]. During the process of autophagosome formation, LGG-1 plays a crucial role in structural maintenance, making it a valuable marker for monitoring autophagic activity [57].

α- and β-Amyrins have been shown to participate in the LGG-1-related autophagy pathway by enhancing LGG-1 expression and increasing the number of localized LGG-1 spots. These compounds have demonstrated the ability to protect dopaminergic neurons by reducing cell damage and preventing α-synuclein aggregation, both of which are associated with Parkinson's disease symptoms [58]. Anti-Parkinsonian activities are closely linked to the regulation of cholesterol metabolism, as sterol-mediated cholesterol metabolism plays a significant role in neurological diseases. Low levels of LDL-C are often associated with a higher incidence of Parkinson's disease. α- and β-Amyrins have been shown to regulate cholesterol metabolism, supporting their potential anti-neurological and anti-dementia effects. This suggests that α- and β-amyrins could be promising agents for the treatment of Parkinson's disease [59].

3.8. Anticancer Potential of α- and β-Amyrins

Because of constant demand to develop new, effective and affordable anti-cancer drugs. The traditional medicinal system is a valuable and alternative resource for identifying novel anti-cancer agents. The study is to investigate the inhibitory activity of the compounds of methanolic bark extract of *Shorea robusta* on hepatocellular carcinoma by molecular docking studies on isolated α- and β-amyrins compounds. These compounds are used for docking on human oncogene protein. Docking studies of designed compounds were carried out using molecular docking servers. The recorded for

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alpha and beta amyrin binding with human Ras protein was -9.36 kcal/mol and - 8.90 kcal/mol respectively. Frontier singly occupied molecular orbitals (SOMO) were studied by Density functional theory (DFT) and time dependent-DFT calculations. Among the calculated band gap energies, the β-MOs of α- and β-amyrins compounds have very narrow band gap (-1.057eV). These ndings enlighten the anticancer activities of alpha and beta amyrin in *Shorea robusta* [60].

This study aims to evaluate the chemical composition of *P. heptaphyllum* resin and cytotoxicity on a breast cancer cell line (MCF-7). The chemical composition of the resin was determined by Gas Chromatography coupled to a Mass Spectrometer. Cytotoxicity was evaluated using an MTT assay. Annexin V-FITC, caspase-3, Angiotensin Converting Enzyme activity and Tumor Necrosis Factor alpha (TNF-α) assays were performed to evaluate apoptosis and inflammatory events. The resin consisted of triterpenes, such as α- and β-amyrin. Cytotoxicity was only observed in fractions enriched with α- and β-amyrin. The resin and fractions elicited antiproliferative activity, increased activity of caspase-3 and ACE, and a decrease in the TNF-α level. Altogether, the resin and fractions enriched with α- and β-amyrin promoted cytotoxicity and apoptosis [61].

α- and β-Amyrins have been studied to exhibit significant pharmacological properties. This study was conducted to investigate the anticancer and pro-apoptotic effects of β-amyrin against HepG2 liver cancer cells. The antiproliferative potential of α- and β-amyrins were evaluated using the MTT assay. Apoptosis was assessed through DAPI staining, and DNA damage was analyzed using the comet assay. Cell cycle analysis was performed using flow cytometry, and protein expression levels were assessed by western blotting. β-Amyrin exhibited significant anticancer activity against Hep-G2 liver cancer cells, with an IC_{50} value of 25 μM. The anticancer effects of α- and β-amyrins were attributed to the induction of apoptosis and G2/M phase cell cycle arrest in a dose-dependent manner. Based on the results of the current study, α- and β-amyrins may represent a promising lead compound for the treatment of liver cancer [62].

The anticancer activity of α- and β-amyrins have been evaluated in various therapeutic combinations against colon cancer, aiming to identify the key mechanisms involved in mitigating nickel-induced carcinogenesis. To evaluate the ligand–protein interactions of four selected compounds with Vascular Endothelial Growth Factor (VEGF), Matrix Metalloproteinase-9 (MMP-9), and Interleukin-10 (IL-10), a molecular docking approach was employed using the PyRx bioinformatics tool. Ten rats, each weighing between 160–200 g, were administered intraperitoneal injections of nickel at a dose of 1 ml/kg once per week for three months. Following this exposure, the rats were treated with β-amyrin at a dose of 100 mg/kg body weight for one month. Correlation analysis was performed using Pearson's correlation matrix. All parameters were significantly elevated in the positive control group, indicating pronounced inflammation. The study concluded that α- and β-amyrins are potent anticancer agents capable of targeting cancer biomarkers and hold promise as a superior therapeutic approach against colon cancer in the near future [63].

Natural α- and β-amyrins were isolated from the endemic Brazilian plant *Esenbeckia grandiflora* Mart., and eight synthetic derivatives were subsequently obtained through esterification with bromoacetate, followed by treatment with various amines. The structures of all compounds were confirmed through analysis of ^{1}H and ^{13}C nuclear magnetic resonance (NMR), Fourier-transform infrared spectroscopy (FTIR), and high-resolution mass spectrometry (HRMS) data. The synthetic derivatives were evaluated for their cytotoxic activity against human tumor cell lines, including PC3 (prostate carcinoma), HCT-116 (colon carcinoma), and HL60 (leukemia). The HCT-116 and PC3 cell lines exhibited weak tumor growth inhibition, with inhibition ranges of 13.9–25.4% and 10.3–28.8%, respectively. In contrast, the derivatives demonstrated moderate cytotoxic activity against the HL60 leukemia cell line, with inhibition ranging from 13.6% to 59.0% [64].

α- and β-Amyrins were found to be highly active and non-toxic compounds against tumor cells. Their inhibitory effects were tested on four human tumor cell lines (HL-60, MDAMB-435, SF-295, and HCT-8), as well as on normal peripheral blood mononuclear cells (PBMCs). The results demonstrated that α- and β-amyrins exhibited significant anticancer activity while showing minimal toxicity to normal cells, making them promising candidates for further exploration in cancer therapy [65].

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HeLa cells were treated with β-amyrin, and the cells were pretreated with 100 μM N-acetyl-L-cysteine for 1 hour before treatment. The efficacy of β-amyrin was evaluated through antiproliferative activity measured by the MTT assay, genotoxicity using the micronucleus assay, and the determination of reactive oxygen species (ROS), nitric oxide (NO), and caspase-3 levels using fluorescence spectrophotometry and a colorimeter. Protein expression was assessed via immunoblotting. β-Amyrin (10-200 μM) inhibited the growth of cancer cells with IC_{50} values ranging from 10 to 100 μM. Western blot analysis revealed that β-amyrin induced apoptosis-related proteins, including Bcl-2, caspase-3, caspase-9, phospho-p38 mitogen-activated protein kinase (MAPK), and phospho-Jun N-terminal kinase (JNK) in cancer cells. Genotoxic effects were observed following β-amyrin treatment, and HeLa cells exhibited a significant increase in total ROS. Protein expression analysis showed that β-amyrin upregulated MAPK-p38, phospho-JNK, and growth arrest and DNA damage-inducible β (GADD45β) in HeLa cells. These results suggest that β-amyrin induces apoptosis through a ROS-mediated mechanism by activating p38 MAPK and JNK pathways via the transcription factor GADD45β, which plays a major role in suppressing the growth of cervical cancer cells [66].

The mixture of α-amyrin and β-amyrin demonstrated anti-cancer potential against the MCF-7 breast cancer cell line with an IC_{50} value of 28.45 μg/mL. Importantly, this compound was not cytotoxic to normal cells, suggesting a selective action against cancer cells. These findings position α- and β-amyrin as promising candidates for developing treatments for breast cancer, with potential for fewer side effects due to their selective cytotoxicity [67].

The mixture of α-amyrin and β-amyrin, isolated from the *Dichloromethane* extract, exhibited significant antitumor activity against several cancer cell lines, including KB-oral, and NCI-H187, with IC_{50} values of 18.01 and 18.42 μg/mL, respectively. Additionally, α-amyrin and β-amyrin demonstrated strong antibacterial activity against *Escherichia coli*, with a minimum inhibitory concentration (MIC) of 31.25 μg/mL. These findings highlight the dual potential of α- and β-amyrin as both anticancer and antibacterial agents [68,69].

The study on α-amyrin and β-amyrin from *Mesua ferrea* stem bark demonstrated their significant in vitro anticancer activity against human colon cancer HCT116 cells. The compounds were tested using the MTT assay, which revealed their toxicity against various cancer cell lines, while also indicating their selective action, as they did not show similar toxicity to normal cell lines. This further supports the anticancer potential of α-amyrin and β-amyrin as promising therapeutic agents for cancer treatment [70].

α-amyrin and β-Amyrin loaded nano capsule for intestinal delivery and evaluate, preliminarily, its cytotoxic ability against leukemic cells. Nano capsule formulations were designed by the solvent displacement-evaporation method. The cytotoxic potential of the nano capsules was evaluated in vitro using different leukemic lineages. Nano capsules coated with Kollicoat® Mae 100 P presented the smallest particle size (130 nm), the lowest zeta-potential (−38 mV), and the narrowest size distribution (PdI = 0.100). The entrapment efficiency was 65.47%, while the loading capacity was 2.40%. Nano capsules release 100% of α-amyrin in 40 min (pH 7.4), by using a possible mechanism of swelling-diffusion. The formulation showed excellent on-shelf physicochemical stability for one year. Additionally, nano capsules produced a selective cytotoxic effect on a human leukemia lineage Kasumi-1, an acute myeloid leukemia cell line, and produced cell death by apoptosis. α-amyrin-loaded nano capsules appear to be a promising nano formulation that could be used against leukemia [71].

3.9. The Potential Antibacterial of α- and β-Amyrins

The mixture of α- and β-amyrins isolated from *Protium heptaphyllum* demonstrates significant antibacterial activity against *Escherichia coli* and *Staphylococcus aureus* strains, including multidrug-resistant strains. Additionally, these compounds effectively inhibit efflux resistance mechanisms in *S. aureus* strains 1199B and K2068, which carry the NorA and MepA efflux pumps. α- and β-amyrins showed a higher affinity for these efflux pumps (NorA and MepA) compared to commonly used antibiotics like ciprofloxacin and norfloxacin. This suggests that α- and β-amyrins may enhance antibiotic activity by inhibiting efflux pumps, thus preventing bacteria from expelling the antibiotics.

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These findings support the potential of α- and β-amyrins as promising antibacterial agents, especially when combined with conventional antibiotics, to combat multidrug-resistant infections [72].

The study demonstrated that the mixture of α- and β-amyrin isolated from *Morinda lucida* leaves exhibited strong antibacterial activity against multidrug-resistant strains of Enterobacteriaceae, including *Klebsiella, Pragia, Serratia, Enterobacter, Providencia*, and *E. coli*. The compound mixture showed inhibition zones ranging from 15 to 18 mm at a concentration of 0.093 µg/ml. These results suggest that α- and β-amyrins from *M. lucida* could be potent agents for treating infections caused by antibiotic-resistant bacteria. This supports the traditional use of *M. lucida* in herbal medicine, and these compounds may offer alternative or complementary treatment for infectious diseases that are resistant to conventional antibiotics [73].

The study demonstrated that the α- and β-amyrin fraction (3.4 mg/mL) from *C. trichotomum* exhibited significant antibacterial activity against *E. coli*, *S. aureus*, and *H. pylori*. The compounds showed inhibition zones of 12 mm against *E. coli* and 13 mm against *H. pylori*, indicating their potential as antibacterial agents. At a lower concentration of 1.7 mg/mL, α- and β-amyrins still showed inhibition against *H. pylori*, with inhibition zones of 10 mm and 11 mm, respectively. These findings suggest that α- and β-amyrins from *C. trichotomum* could serve as promising therapeutic agents against infections caused by these bacterial strains, offering a potential alternative to traditional antibiotics [74].

3.10. The Potential Anti-HIV of α- and β-Amyrins

The potential of α- and β-amyrins in combating HIV has been studied with promising outcomes. These compounds were extracted from the stems and roots of *Kadsura lancilimba.* Their structures and stereo chemistries were identified primarily from mass and NMR spectral data. α- and β-Amyrins inhibited HIV replication with an (IC_{50} : 1.4 µg/mL). α- and β-amyrins have shown antiviral activity, particularly against HIV, making them a significant discovery in the pursuit of treatments for this "disease of the century." Their therapeutic potential could be a step forward in developing alternative treatments for HIV, especially given the ongoing need for more effective antiviral drugs [75]. This underscores the urgent need for safer, more effective drugs to combat resistant strains and advance acquired immunodeficiency syndrome (AIDS) therapeutics. α- and β-Amyrins were identified from *Uncaria rhynchophylla* hooks. These compounds exhibited potent inhibition of HIV-1 protease (PR), one of the essential enzymes in the virus's life cycle, with 3β-hydroxy-27-p-Z-coumaroyloxyurs-12-en-28-oic acid (8) showing the most potent inhibitory activity. In silico docking the result of triterpene ester 8 elucidated conventional hydrogen bonding with specific amino acid residues-Asp29B, Lys45B, and Asn25A interacting with the aromatic hydroxyl group at position 7 and the carboxylic acid at position 28. Additionally, these interactions occur via π–anion and π–alkyl and alkyl hydrophobic interactions, which are responsible for the compound's mode of action. These molecular docking studies strongly confirmed an excellent SAR. The study suggests that triterpene esters from *U. rhynchophylla* could represent a new class of potent HIV-1 PR inhibitors with less toxicity, suitable for combination antiretroviral therapy for AIDS [76]. The isolation of α- and β-amyrins, along with 10 other triterpene compounds, from *Stauntonia obovatifoliola Hayata subsp* represented a significant step in the search for potential anti-HIV agents. Through the analysis of high-resolution EI/FAB-MS spectral data and 1D and 2D NMR spectra, the structures of these compounds were elucidated. Notably, α- and β-amyrins, along with other compounds from this plant, demonstrated HIV-1 protease inhibitory activity in studies. This discovery highlighted the potential of these triterpenes as promising candidates for the development of novel anti-HIV therapies. Further, emphasized their importance in addressing the ongoing global HIV/AIDS epidemic [77]. α- and β-Amyrins, isolated from the leaves and twigs of *Gardenia carinata*, were structurally characterized using spectroscopic methods. These triterpenoids exhibited notable biological activities, specifically anti-topoisomerase IIα and anti-HIV-1 properties. Remarkably, α- and β-amyrins were found to be completely non-cytotoxic, indicating their potential as safe therapeutic agents. The ability of these compounds to inhibit topoisomerase IIα, an enzyme critical in DNA replication and transcription, alongside their

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anti-HIV-1 activity, positions them as promising candidates for further research in the development of novel treatments for cancer and HIV, with minimal toxicity [78].

α- and β-Amyrins isolated from *Cassine xylocarpa* stem and *Maytenus cuzcoina* root bark were studied for their anti-HIV potential. The structures of these compounds were elucidated using 1D, 2D NMR techniques. To enhance their anti-HIV activity, derivatives of α- and β-amyrins were synthesized through chemical modification of the parent compounds. These modified derivatives exhibited inhibitory effects on HIV replication, with IC_{50} values (4.08, 4.18, 1.70 μM) in the micromolar range. This indicates their strong potential as anti-HIV agents. The findings support the idea that α- and β-amyrins, both in their natural form and as modified derivatives, could be developed as valuable therapeutic agents for the treatment of HIV [79]. α- and β-Amyrin derivatives have demonstrated potent anti-HIV activity, with the derivatives being specifically characterized based on their C-3 configuration. This study aimed to explore how modifications to the C-3 position and the overall triterpene backbone influence their anti-HIV effectiveness. The results provided valuable insights into the structure-activity relationship of α- and β-amyrins, highlighting how changes in the chemical structure can enhance their ability to inhibit the growth of HIV cells. This research further identifies α- and β-amyrins, particularly their modified derivatives, as promising candidates for the development of anti-HIV therapies. The study emphasizes the importance of structural modifications in improving the efficacy of natural compounds in combating complex diseases like HIV [80].

3.11. The Isolation α- and β-Amyrins

The extraction of α- and β-amyrins from *C. hindsii* has proven highly effective, yielding a remarkable amount of 10.75 g/kg dry weight. This highlighted *C. hindsii* as a valuable source of raw material for α- and β-amyrins extraction. The identification and structural elucidation of the isolated compounds were carried out using advanced techniques such as gas chromatography-mass spectrometry (GC-MS), electrospray ionization-mass spectrometry (ESI-MS), and nuclear magnetic resonance (NMR). These methods enabled accurate characterization of the compounds and confirmed the effectiveness of the extraction process, thereby reinforcing *C. hindsii* as a promising source of bioactive triterpenoids [23].

4. Discussion

As the global population grows and life expectancy increases, the burden of both chronic and infectious diseases is escalating. This makes the development, accessibility, and sustainability of pharmaceutical resources more critical than ever. In this context, identifying effective bioactive compounds like α- and β-amyrins from natural sources becomes a key strategy. These compounds not only offer therapeutic promise but also align with the increasing interest in plant-based and sustainable drug development [87]. Pharmaceuticals are therapeutic products derived from organic or inorganic compounds that play a crucial role in protecting human health and combating a wide range of diseases. With the growing demand for effective and sustainable treatments, the exploration of bioactive natural compounds, such as α- and β-amyrins, offers promising avenues for the development of novel pharmaceuticals that can address both current and emerging health challenges [88]. The pharmaceutical industry has always demanded rigorous standards and meticulous testing of all input materials to ensure safety, efficacy, and quality in the development of therapeutic products [89]. According to statistics from the World Health Organization, global demand for pharmaceuticals increased steadily at an annual rate of 5.8% from 2014 to 2017 [90]. Musculoskeletal drug groups have consistently played a significant role, accounting for the highest share of approximately 14% of global pharmaceutical demand in 2017 [91]. Cardiovascular drugs ranked second in global pharmaceutical demand, followed by anti-cancer drugs in third place and anti-infectives in fourth. The fifth-largest segment is the pharmaceutical market for treating metabolic disorders such as diabetes, as well as thyroid and pituitary diseases. Notably, this segment is projected to be the fastest-growing area in the global pharmaceutical market [92]. The demand for pharmaceuticals is projected to grow steadily at an annual rate of 9-11.6% in the coming years [93].

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Worldwide pharmaceutical consumption is rapidly increasing due to the rising prevalence of chronic diseases, an aging population, and the growing need for clinical management [94]. According to data from the Organization for Economic Cooperation and Development (OECD), global demand for cholesterol-lowering drugs nearly quadrupled, the use of antidepressants doubled, and the consumption of antihypertensive and antidiabetic drugs nearly doubled between 2000 and 2015 [95, 96]. Not only is the demand for pharmaceuticals increasing in quantity, but there is also a growing demand for improved quality and variety. Medications for diabetes, hypertension, acquired immunodeficiency syndrome (AIDS), malaria, and tuberculosis are among those seeing a significant rise in demand. As economies grow, so too does the need for medicines, healthcare services, and broader insurance coverage [97]. The global population growth is also a major factor contributing to the increasing demand for pharmaceuticals [98]. The COVID-19 pandemic of 2020 served as a stark reminder of the critical need for pharmaceuticals. It highlighted the importance of continuously developing and preparing medical solutions to address unexpected changes or pandemics [99]. As society has developed, the demand for pharmaceuticals, healthcare, and protection has increasingly focused on meeting more complex needs [100]. Therefore, researching and developing the value of α- and β-amyrins to serve the global pharmaceutical industry will hold significant importance.

The pharmacological activities of the α- and β-amyrin mixture have been extensively studied in both preclinical and clinical settings to support future medicinal applications. Research has demonstrated that α- and β-amyrin possess a wide range of therapeutic properties, including analgesic, anti-inflammatory, anticonvulsant, antidepressant, gastroprotective, hepatoprotective, anti-pancreatitis, antihyperglycemic, and hypolipidemic effects. Notably, these compounds have been shown to be non-toxic to normal cells. Therefore, α- and β-amyrin represented a promising source of raw materials for the development of future medicinal products [101]. α- and β-Amyrin have also been shown to exhibit anti-cancer and anti-inflammatory properties [102], cardiovascular disease, diabetes and arthritis [103]. Inflammation is a biological response of the body to external agents such as microorganisms, chemical substances, and physical injuries, as well as internal factors like tissue necrosis, metabolic disturbances, and immune reactions [104]. Common symptoms of localized inflammation include swelling, heat, redness, and pain. In contrast, internal inflammation, which is not visible to the naked eye, may manifest in conditions such as hepatitis, appendicitis, colitis, gastritis, encephalitis, and nephritis [105]. One of the most serious inflammatory diseases is pneumonia. It is primarily caused by the accumulation of fluids in the lungs and the narrowing of the airways, which leads to difficulty in breathing. Pneumonia is often associated with infections and may also be related to underlying conditions such as asthma or chronic obstructive pulmonary disease (COPD) [106]. Periodontal disease is a common form of inflammation that affects the gums, leading to gum recession and deterioration of the bone structure supporting the teeth [107]. Inflammation can negatively affect bone health by disrupting bone growth and accelerating bone loss. Specifically, inflammation of the digestive system can compromise bone integrity by impairing the absorption of essential nutrients such as calcium and vitamins that are vital for bone development and maintenance [108]. Inflammation has also been linked to depression, contributing to symptoms such as mood swings, loss of appetite, and sleep disturbances [109]. Inflammation of the gut can trigger immune cells to react to the bacteria already present in the digestive system, leading to chronic inflammation. This ongoing immune response can damage the digestive tract, potentially contributing to autoimmune diseases such as inflammatory bowel disease (IBD), Crohn's disease, and ulcerative colitis [110]. Arthritis, particularly rheumatoid arthritis, is a major cause of serious joint damage. This autoimmune disease is also associated with an increased risk of cardiovascular problems [111]. Inflammation has also been linked to cardiovascular disease. When the body is injured or damaged, it triggers inflammation in the blood vessels. The formation of atherosclerotic plaques in the arteries can perpetuate chronic inflammation. These fatty plaques attract white blood cells, causing them to grow larger and potentially leading to blood clots, which increase the risk of cardiovascular disease [112]. Chronic inflammation has been linked to an increased risk of various cancers, including lung, esophageal, cervical, and gastrointestinal cancers. When immune cells

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initiate an inflammatory response, the immune system's regulation becomes compromised, creating a favorable environment for cancer cells to proliferate [113]. Inflammation can negatively impact sleep, either causing difficulty sleeping or leading to excessive sleepiness [114]. α- and β-Amyrin are naturally occurring mixtures of pentacyclic triterpenes with a broad spectrum of biological activities. The interaction between α- and β-amyrin and inclusion complexes (ICs) was confirmed through solid-state physicochemical characterization using techniques such as Fourier transform infrared (FTIR) spectroscopy, scanning electron microscopy (SEM), X-ray diffraction (XRD), thermogravimetry (TG), and differential scanning calorimetry (DSC). The formation of ICs with cyclodextrin suggests that α- and β-amyrin are promising and effective compounds for enhancing anti-inflammatory activity [115]. Thus, inflammation is not merely the body's response to harmful agents; rather, it lies at the core of many serious diseases. This study has demonstrated that the anti-inflammatory potential of α- and β-amyrin opens numerous opportunities for developing drugs to support the treatment of related conditions.

Diabetes is a chronic disease that affects the body's ability to produce or use insulin, a hormone that helps convert glucose into energy [116]. The harmful effects of diabetes on the endocrine system are significant. Specifically, the pancreas plays a crucial role in producing and releasing insulin, which helps convert sugar into energy. If this process is disrupted or the body becomes unable to effectively use insulin, the body turns to fat as an alternative energy source. The byproducts of this process, including acids and ketones, can be toxic. These substances are responsible for both acute and chronic complications associated with diabetes [117]. The accumulation of ketones can lead to diabetic ketoacidosis, which is characterized by symptoms such as increased thirst, frequent urination, fatigue, and fruity-smelling breath. If not detected and treated promptly, ketoacidosis can result in loss of consciousness or even death [118]. Diabetes can lead to kidney damage, impairing the kidneys' ability to filter waste products from the blood. High levels of protein in the urine, known as microalbuminuria, can be an early sign that the kidneys are not functioning properly [119]. Kidney disease related to diabetes is known as diabetic nephropathy. The effects of this condition often do not show symptoms until it has progressed to more advanced stages. People with diabetes should regularly have their kidneys checked, as diabetes can cause irreversible damage, potentially leading to kidney failure [120]. Hyperglycemic hyperosmolar syndrome (HHS) occurs in patients with type 2 diabetes. In this condition, blood sugar levels become extremely high, but ketones do not accumulate. Symptoms include severe dehydration and loss of consciousness. HHS typically develops in individuals with undiagnosed diabetes or those whose diabetes are not well controlled. If left untreated, HHS can lead to serious complications such as heart attack, stroke, or infection [121]. High blood sugar can interfere with the stomach's ability to empty properly, a condition known as gastroparesis. This delay in stomach emptying can further exacerbate hyperglycemia. Diabetes is the leading cause of gastroparesis. Symptoms typically include nausea, vomiting, bloating, and heartburn [122]. High blood sugar, oxidative stress, and inflammation caused by diabetes can lead to endothelial dysfunction, inflammation, and platelet activation and aggregation. Over time, these processes restrict blood flow and increase the risk of blood vessel hardening [123]. Poor circulation can affect the hands and feet, causing pain in the calves while walking (claudication). People with diabetes are particularly susceptible to foot problems due to narrowed blood vessels in the legs and feet, which can result in numbness or a burning sensation. Additionally, diabetic neuropathy can lead to reduced sensation in the limbs, making individuals unaware of injuries or infections [124]. One of the harmful effects of diabetes is the increased risk of developing infections or diabetic foot ulcers. Poor circulation and nerve damage further elevate the risk of requiring a foot or leg amputation. If you have diabetes, it is crucial to take good care of your feet and schedule regular check-ups to prevent complications [125]. Diabetes increases the risk of developing high blood pressure, which places additional strain on the heart. According to the National Diabetes Information Center, people with diabetes are twice as likely to develop cardiovascular disease or experience a stroke compared to those without diabetes. Monitoring and controlling blood sugar, blood pressure, and cholesterol levels can help reduce this risk. Therefore, it is important to adopt healthy eating habits and regular

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exercise routines [126]. Diabetes can lead to various skin problems, including dry skin and skin infections. The harmful effects of diabetes often cause the skin to lose moisture, particularly in the feet, which may become dry and cracked. People with diabetes are also more susceptible to boils, hair follicle infections (folliculitis), swelling, and nail infections. Additionally, diabetes increases the risk of bacterial infections, such as those caused by *Staphylococcus*, compared to individuals without diabetes [127]. Diabetes can damage peripheral nerves, impairing the patient's ability to perceive heat, cold, and pain. As a result, individuals may be unaware of injuries and unable to react appropriately to them [128]. People with diabetes are more likely to develop cataracts at an earlier age than those without diabetes. They are also at higher risk of glaucoma. Additionally, swollen and leaky blood vessels in the eye, a condition known as diabetic retinopathy, can damage vision and even lead to blindness. Common symptoms of diabetic retinopathy include the appearance of floating particles or spots in your vision [129]. Choosing the right methods for treating diabetes is crucial, with the effective regulation of insulin levels being a fundamental aspect. In 2015, approximately 422 million people worldwide were living with diabetes. The number of diabetic patients has been steadily increasing over the years, and each year, around 1.5 million people die from diabetes-related complications [130]. Diabetes results in many serious consequences and poses a significant challenge to global health. Studies conducted both in vivo and in vitro have demonstrated the anti-diabetic potential of α- and β-amyrin (Table 2). These findings highlight the considerable value of α- and β-amyrin and suggest numerous opportunities for developing anti-diabetic drugs.

Table 2. Studies on the Anti-diabetes Potential of α- and β-Amyrins.

Disease	Cell Line (Receptors)	Duration	Doses of α- and β-Amyrins	Assay	References
Diabetes, Cardiovascular	Beta cell	12 hours	10, 30, and 100 mg/kg	Vivo	[29]
Diabetes	Beta cell	24 hours	50 µg/kg	Vivo	[30]
Diabetes	-	-	10 µg/mL	Vitro	[31]
Diabetes	3T3-L1	24 hours	1,10,100 µg/mL	Vivo	[32]
Diabetes	HK-2	24 hours	100µg/kg	Vivo	[33]
	-	-	19.50 µg/mL	Vitro	[34]

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Atherosclerosis occurs when arteries become clogged with plaque, which is made up of fats, cholesterol, calcium, and other substances that accumulate on the walls of the arteries [131]. Atherosclerosis typically doesn't cause symptoms until it reaches an advanced stage. At this point, severe narrowing of the arteries can interrupt blood flow, preventing oxygen and nutrients from reaching vital organs and tissues. This disruption contributes to the development of cardiovascular disease. If an atherosclerotic plaque ruptures and forms a blood clot, it can lead to a heart attack or stroke [132]. Patients with coronary atherosclerosis (affecting the heart) may experience angina and myocardial infarction, which can lead to heart failure if left untreated [133]. Carotid atherosclerosis, which affects the brain, can lead to symptoms of a transient ischemic attack (TIA), which may progress to a stroke if left untreated. Symptoms include sudden weakness or numbness in an arm or leg, slurred speech or difficulty speaking, temporary loss of vision in one eye, or drooping of the eyelid muscles [134]. Atherosclerosis can lead to the development of peripheral artery disease (PAD) in the arms and legs. Symptoms of PAD include decreased blood flow in the affected limb, along with numbness and pain. PAD also increases the risk of stroke or heart attack, and in severe cases, gangrene can develop, potentially leading to amputation [135]. Atherosclerosis can lead to chronic kidney disease by narrowing the arteries that supply blood to the kidneys. This restriction of oxygen-rich blood impairs kidney function, preventing the kidneys from effectively eliminating toxins and excess fluid from the blood [136]. Atherosclerosis has been studied extensively as a cause of many dangerous complications. The strong anti-atherosclerotic potential of α- and β-amyrin has been

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demonstrated in Table 3, opening new opportunities and directions for the development of pharmaceutical products. These findings highlighted the value of α- and β-amyrins in supporting and treating atherosclerosis-related diseases.

Table 3. Studies on the Anti-atherosclerosis Potential of α- and β-Amyrins.

Disease	Cell Line (Receptors)	Duration	Doses of α- and β-Amyrins	Assay	References
Atherosclerosis	HepG2	-	200 μmol/L	Vitro	[35]
Type II diabetes, and atherosclerosis	IL-6, TNF-α	-	0.01 μM	Vitro	[36]
Nonalcoholic fatty liver	Lipid levels	15 weeks	10, 20, 50 mg/kg	Vivo	[37]
Vascular disorders	SVEC4-10	-	0,6 và 0,3 μM	Vitro	[38]
Vascular	HUVECs	24–72 h	0.025–10 μM)	Vitro	[39]
Obesity-	PHE,ACh,SNP	15 days	20 mg/kg	Vivo	[40]

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Nociception is the process by which noxious stimuli are encoded by the sensory nervous system. A series of events and processes are required for an organism to detect a painful stimulus, which is then converted into a molecular signal. This signal is recognized and processed to activate the appropriate response [137]. Nociception causes discomfort and may indicate that tissues are being damaged. To alleviate this, anti-nociceptive treatments are often used. While these treatments may not eliminate pain, they provide relief, helping the patient feel more comfortable [138]. Antinociception drugs are effective in treatment headaches, colds, flu [139]. Antinociception drugs are used muscle pain [140], joint pain [141], back pain due to disc herniation or spinal stenosis [142]. Antinociception is applied to treat physical trauma [143], surgery [144], or childbirth [145], non-steroidal anti-inflammatory pain relievers (NSAIDs): This group of drugs includes drugs such as meloxicam, piroxicam, aspirin, diclofenac, indomethacin, etc. This is a group of drugs used to treat fever, headaches and treat pain, treat colds and sinusitis [146]. Non-steroidal anti-inflammatory pain relievers (NSAIDs) have studied like a novel mechanism of anti-nociception [147]. Paracetamol pain reliever: This is the most popular drug and is the basic pain reliever in treating mild to moderate pain, especially fever reduction [148]. Paracetamol pain reliever is kind of anti-nociception [149]. Thus, α- and β-amyrin have been proven to possess anti-nociceptive properties (Table 4). This indicates that α- and β-amyrin hold significant value, comparable to many other pharmaceuticals, in treating various diseases and complications related to nociception. α- and β-amyrin were considered valuable discoveries in the development of effective pharmaceutical treatments.

Table 4. Studies on the Anti-nociceptive Potential of α- and β-Amyrins.

Disease	Cell Line (Receptors)	Duration	Doses of α- and β-Amyrins	Assay	References
Antinociceptive	Capsaicin, naloxone	10–20 min	10, 30, and 100 mg/kg	Vivo	[41]
Antinociceptive	Protein kinase A, protein kinase C	-	0.1–100 mg/kg)	Vivo	[42]
Visceral pain	KBr pellets, Bruker AC	-	45-90%	Vitro	[43]
Novel analgesic	CHO-K1 cell, Cannabinoid CB1 and CB2 receptors	-	> 10μM	Vitro	[44]

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Gout is a common form of arthritis characterized by sudden and severe pain in the joints, particularly in the toes, fingers, and knees. The affected joints become red, swollen, and extremely painful, often making it difficult for patients to walk [150]. Gouts occur in individuals who have elevated levels of uric acid in their blood. Uric acid is a chemical produced when the body breaks down certain foods. When uric acid levels become too high, it can form sharp, needle-like crystals that accumulate in the joints, causing intense pain and inflammation [151]. Uric acid crystals can accumulate in the tubes that carry urine from the kidneys to the bladder, leading to the formation of kidney stones. This buildup can cause painful urination and other urinary problems [152]. Tophi are deposits of urate crystals that form around joints in people with long-term gout. These crystals appear as nodules, bulging underneath the skin in areas such as the feet, knees, wrists, fingers, and heel tendons [153]. Tophi are visible to the naked eye and can be felt beneath the skin. The areas surrounding the tophi are often hot, soft, swollen, and painful. This swelling can limit joint movement, reducing the range of motion and causing significant difficulty in daily activities [154]. Chronic gouty arthritis can result in permanent joint damage, leading to deformity and stiffness. This can significantly impact on the patient's long-term mobility. In severe cases, surgery may be required to correct joint deformities [155]. Excessive uric acid levels in the body can lead to kidney stones in 2 out of 10 people with gout. The kidneys, which filter waste from the blood, also filter uric acid. When uric acid levels remain elevated over a prolonged period, urate salts can precipitate, leading to the formation of uric acid stones in the kidneys [156].

Gouts can lead to kidney disease and eventual kidney failure due to the formation of uric acid kidney stones. As stone masses grow, they increase the risk of kidney damage, potentially leaving scars that impair kidney function. Over time, this can progress to kidney failure [157]. Gout complications can also include bone fractures. Gout increases the risk of fractures by negatively affecting bone properties due to inflammation and swelling caused by uric acid crystal deposition. The development of tophi further contributes to bone damage and erosion. Over time, prolonged gout can weaken bones, increasing the risk of osteoporosis and making patients more susceptible to bone fractures [158]. Cardiovascular diseases present a significant risk for people with gout. While gout does not directly cause cardiovascular disease, studies show that individuals with gout are twice as likely to experience a heart attack or stroke compared to those without the condition. This increased risk is linked to uric acid, which leads to the accumulation of urate crystals and the formation of blood clots. These clots are a direct contributor to the heightened risk of heart attack and stroke. Gout-related cardiovascular complications are particularly dangerous, as patients are at twice the risk of death from heart failure compared to those without gout [159]. Many people with gout experience sleep disturbances because gout pain often flares up at night. The intensity of the pain can cause significant discomfort, sometimes waking the patient from sleep. In cases where the pain is persistent and continuous, it may prevent the patient from falling back to sleep, leading to serious health declines. Additionally, the complications of gout can contribute to fatigue, stress, and a range of other health issues associated with insomnia [160]. Reduced bone density is a common complication of gout, resulting from bone damage and decreased bone function. Bone density refers to the amount of mineral tissue in the body, measured per unit area (g/cm^2), and is used as an indicator of bone quality. Lower bone density increases the risk of bone-related issues such as osteoporosis. People with gout often experience reduced bone density due to joint inflammation and the formation of tophi particles, which directly damage the bones. This increases the risk of other bone and joint conditions, including osteoporosis, osteoarthritis, and bone fractures [161]. People with gout often experience reduced bone density due to joint inflammation and the presence of tophi particles, which directly damage the bones. This increases the risk of other bone and joint conditions, including osteoporosis, osteoarthritis, and bone fractures [162]. The harmful effects of gout on human life and health are concerning. The discovery of the anti-gout potential of α- and β-amyrin (Table 5) is considered a significant breakthrough in the development of pharmaceuticals that can effectively treat this condition.

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Table 5. Studies on the Anti-gout Potential of α- and β-Amyrins.

Disease	Cell Line (Receptors)	Duration	Doses of α- and β-Amyrins	Assay	References
Gout	XO	-	258.22 μg/mL	Vitro	[23]
Gout	XO, Urate crystals	-	-	Vivo	[45,46]
Gout	NTUB1	24 hours	-	Vitro	[47]

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Sedatives work by slowing down brain activity, helping to calm and regulate the nervous system. These drugs have a direct effect on the central nervous system, either stimulating or inhibiting nerve activity to prevent and treat various conditions [163]. Insomnia is a type of sleep disorder that manifests in various forms, including difficulty falling asleep, trouble staying asleep, waking up too early despite not getting enough rest, and being unable to return to sleep after waking [164]. Insomnia can be a symptom of underlying mental health conditions [165]. The positive effects of α- and β-amyrin on the nervous system, including sedation and promoting better sleep, are considered among its greatest values (Table 6). These findings have shown the promising potential of this compound in the development of pharmaceuticals and functional foods aimed at sedatives, sleeping aids, and supporting or stimulating the nervous system.

Table 6. Studies on the Positive Effects of α- and β-Amyrins on Nerves.

Disease	Cell Line (Receptors)	Duration	Doses of α- and β-Amyrins	Assay	References
Insomnia	GABAergic	12 hours	1, 3, or 10 mg/kg	Vivo	[48]
Convulsant, Sedative, Anxiolytic	Glutamate, Aspartate, taurine	12 hours	2.5; 5; 10; 25 μg/mL	Vitro	[49]
Analgesia	TRPV1, Opioid	12 hours	3 - 100 mg/kg	Vivo	[50]
Sedative, Depressant	TRPV1, Ruthenium red	15 hours	5, 10, 20 mg/kg	Vivo	[51]
Alzheimer	pPI3K, PI3K, pAkt, Akt	24 hours	4 μg/mL	Vitro	[52]
Protective central and peripheral nervous systems	Triglycerides	-	2000 mg/kg	Vivo	[52]

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Parkinson's disease is a neurological disorder that typically occurs when a group of brain cells degenerate, impairing the brain's ability to control muscle movements. This leads to difficulties in walking, slow leg movements, and hand tremors. As the disease progresses, it can affect nerve cells, leading to a deficiency of dopamine, a key neurotransmitter involved in motor control [166]. Progressive Parkinson's disease can increase the risk of death, particularly as symptoms such as hallucinations, cognitive decline, worsening motor disability, comorbidities, and prolonged disease duration become more severe [167]. Individuals with advanced Parkinson's disease may experience falls, pressure ulcers, difficulty swallowing, and weakness. These complications are associated with an increased risk of early death [168]. Thus, finding effective pharmaceuticals to treat Parkinson's disease is an urgent need. The results demonstrating the potential of α- and β-amyrin in treating Parkinson's disease (Table 7) offered promising opportunities to develop pharmaceuticals that can support and treat this condition.

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Table 7. Studies on the Anti-Parkinsonian Potential of α- and β-Amyrins.

Disease	Cell Line (Receptors)	Duration	Doses of α- and β-Amyrins	Assay	References
Parkingson	6-OHDA	72 hours	5, 10, 15, 30 μM	Vitro	[54]
Parkingson	LGG-1	12 hours	5-30μM	Vitro	[55]
Parkingson	LGG-1	-	-	Vitro	[57]
Parkingson	LGG-1	-	-	Vitro	[58]
Parkingson	LDL-C	-	-	Vitro	[59]

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Table 8. Studies on the Anticancer Potential of α- and β-Amyrins.

Disease	Cell Line (Receptors)	Duration	Doses of α- and β-Amyrins	Assay	References
Liver cancer	Hepatocellular	-	-9.36 - 8.90 kcal/mol	Docking	[60]
Breast cancer	MCF-7, ATCC-HTB22	72 hours	2.35-2.48 μg/ml	Vitro	[61]
Liver cancer	Hep-G2	-	25 μM	Vitro	[62]
Colon cancer	VEGF, MMP-9, IL-10	30 days	100 mg/kg	Vivo	[63]
Prostate carcinom cancer	PC3, HL60	72 hours	13,9-25,4%	Vitro	[64]
Leukemia cancer	HL-60, MDAMB-435, SF-295 and HCT-8	-	1.8 - 3 μM	Vitro	[65]
Cervical cancer	HeLa	-	10-200 μM	Vitro	[66]
Breast cancer	MCF-7	-	28.45 μM	Vitro	[67]
Skin cancer	KB-oral	-	18.01 μM	Vitro	[68,69]
Lung cancer	NCI-H187		18.42 μM	Vitro	[68,69]
Colon cancer	HCT116	-	-	Vitro	[70]
Leukemia cancer	Kasumi-1	1 year	-	Nano	[71]

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Table 9. Studies on the Antibacterial Potential of α- and β-Amyrins.

Bacterial	Receptors	Doses of α- and β-Amyrins	Assay	References
Escherichia coli, Staphylococcus aureus	NorA, MepA	-	Docking	[72]
Klebsiella, Pragia, Serratia, Enterobacter, Providencia, and *E. coli.*	Inhibition zones	0.093 μg/ml	Vitro	[73]
E. coli, S. aureus, H. pylori	Inhibition zones	3.4 mg/mL	Vitro	[74]

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Table 10. Studies on the Anti-HIV Potential of α- and β-Amyrins.

Disease	Research Subject (Receptors)	Doses of α- and β-Amyrins	Assay	References
HIV	NMR spectral-	1.4 μM	Vitro	[75]
HIV	SAR of HIV-1 PR inhibitors	0.34 μM	Vitro	[76]
HIV	HR-EI/FAB-MS and 1D and 2D NMR	-	Vitro	[77]
HIV	A549	0.6–4.8 μM	Vitro	[78]
HIV	1D and 2D NMR	4.08, 4.18, 1.70 μM	Vivo	[79]
HIV	C-3 pharmacophore	0.0006 μM	Vitro	[80]

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Table 11. The Source Quantification of α- and β-Amyrins.

Source of Extraction	Extraction Efficiency (g/kg dry weight)	References
Protium kleinii	2.40	[81]
Symplocos cochinchinensis	1.70	[82]
Swertia longifolia	2.0	[83]
Melastoma malabathricum	0.60	[84]
Swertia longifolia	1.00	[85]
Canarium tramdenum	1.52	[86]
Celastrus hindsii	10.75	[23]

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Cancer is a group of diseases that can originate in various organs and tissues throughout the human body. It is classified as a malignant condition characterized by the rapid and uncontrolled growth of abnormal cells. These cells grow beyond the normal regulatory boundaries of the body and can invade nearby tissues. When cancer spreads to other parts of the body through the bloodstream or lymphatic system a process known as metastasis it leads to complex complications and is a major cause of death [169]. Cancer is considered the most dangerous disease worldwide, causing approximately 10 million deaths each year, about 20% of all global deaths. The primary risk factors linked to cancer include unhealthy lifestyle and work habits, such as excessive alcohol consumption, smoking, physical inactivity, and diet low in vegetables. The most diagnosed cancers include lung cancer, colorectal cancer, liver cancer, rectal cancer, breast cancer, and prostate cancer. Many of these cancers can be successfully treated if detected early and managed with appropriate therapies. Recent studies have highlighted the potential of natural compounds such as α- and β-amyrins as promising agents in cancer treatment, offering new avenues for pharmaceutical development [170].

Cancer is the leading cause of death worldwide, with the number of new cases and cancer-related deaths continuing to rise each year (Table 12) [171]. Cancer is recognized as the leading cause of death worldwide, posing a major challenge to global public health. In 2020 alone, there were approximately 18 million new cancer diagnoses and 10 million cancer-related deaths. According to the World Health Organization (WHO), cancer is the second leading cause of death after cardiovascular diseases in 112 countries and territories. As a result, the search for effective cancer treatments has become a global priority, holding significant implications for both economic and social development across nations [172]. Liver cancer is one of the most common and deadly malignancies worldwide, with approximately 800,000 new cases and 700,000 deaths reported each year. It is especially prevalent in regions such as the United States, sub-Saharan Africa, East Asia, and Southeast Asia. The primary risk factors associated with liver cancer include excessive alcohol consumption, smoking, obesity, type 2 diabetes, and exposure to carcinogens like aflatoxin [173]. Therefore, the identification of the anti-liver cancer potential of α- and β-amyrins is considered a significant

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breakthrough in the treatment of this disease [174]. The overall incidence of cancer is expected to be two to three times higher in some countries. Globally, the cancer burden is projected to reach 28.4 million cases by 2040, representing a 47% increase from 2020. Therefore, research and development of effective and targeted drugs is crucial to addressing this global health challenge [175]. The world is currently facing serious challenges due to the rising burden of cancer. Therefore, the discovery and development of effective cancer treatments has become an urgent global priority [176]. α- and β-Amyrins have demonstrated strong anti-cancer activities (Table 8), making them highly valuable compounds. These research findings played an important role in the development of pharmaceuticals and functional foods aimed at supporting and treating various types of cancer.

Table 12. Cancer situation of the world in 2020 [171].

New Cases of Cancer		Cancer Deaths	
Type of Cancer	**Number of People**	**Type of Cancer**	**Number of People**
Breast	2.26 million	Lung	1.80 million
Lung	2.21 million	Colon and rectum	916 000
Colon and rectum	1.93 million	Liver	830 000
Prostate	1.41 million	Stomach	769 000
Skin	1.20 million	Breast	685 000
Stomach	1.09 million		

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Bacteria are responsible for many human diseases, and they can be transmitted through various routes such as ingestion, inhalation, or close contact. Once infected, the human immune system may become compromised, making the body more vulnerable to bacterial proliferation and disease progression [177]. The harmful effects of bacteria can be extremely serious and dangerous, as they can thrive and multiply rapidly in various environments. Moreover, due to their microscopic size, bacteria cannot be seen with the naked eye. This makes it even more important for us to study infectious diseases caused by bacteria and to implement effective prevention measures [178]. Since the discovery of bacteria, it has become clear that they pose a significant danger to humans, causing and spreading various diseases. There is no part of the human body that is immune to bacterial infection [179]. Bacteria can multiply in your body and release toxins that can damage your body's tissues and make you feel sick [180]. Sore throats, staphylococcal infections, cholera, tuberculosis, and food poisoning are all caused by bacteria [181]. Bacteria are extremely dangerous causes of diseases and health problems of humans [182]. Indeed, any organ or part of the body can be vulnerable to bacterial infections. The respiratory tract is particularly susceptible, with bacteria such as *Staphylococcus*, *Streptococcus*, *Pneumococcus*, *Pus Bacillus*, *Whooping Cough*, and *Diphtheria* being common culprits. These bacteria can cause a wide range of respiratory illnesses, and in the case of *Diphtheria*, it can lead to life-threatening complications like acute heart failure or laryngeal diphtheria, especially in children. If left untreated, these bacterial infections can progress rapidly and be fatal [183]. In the digestive tract, there is a powerful army of bacteria that cause disease and cause epidemics such as *E. coli, dysentery bacteria (Shigella), typhoid bacteria (Salmonella), and cholera bacteria* [184].

Table 13. Groups of diseases caused by bacteria.

Related Diseases	Type of Bacteria	Reference
Respiratory	*Staphylococcus*	[185]
	Pneumococcus	[186]
	Diphtheria	[187]
	Streptococcus	[188]
	Pus bacillus	[189]
Digestive tract	*E. coli*	[190]
	Dysentery	[191]

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	Typhoid	[192]
	Cholera	[193]
Genitourinary tract	*E. coli*	[194]
	Proteus	[195]
	Mycoplasma	[196]
	Chlamydia	[197]
	Gonorrhea	[198]
Skin	*Blue pus bacillus*	[199]
	Syphilis	[200]

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In the urinary and genital tracts, there are countless types of bacteria that cause disease and spread to others such as *E. coli, Proteus, Mycoplasma, Chlamydia, and gonorrhea* bacteria. Bacteria that cause diseases in the skin and soft tissues such as *blue pus bacillus, syphilis* [201]. This research has shown that the finding drugs to support and treat diseases related to bacteria, are very important. The antibacterial activities of α- and β-amyrins shown in (Table 9) that guided the useful value of α- and β-amyrins in the production of antibiotics to support and treat related diseases of bacteria. The medicinal potential of α- and β-amyrins has been well established. In addition to their known therapeutic benefits, their antioxidant, antigout, and anti-tyrosinase activities have demonstrated further validate their pharmacological value [23]. Notably, a specialized extraction method detailed in Table 11 yielded the highest reported quantities of α- and β-amyrins globally. These findings collectively highlighted and reinforced the significant value of these compounds for pharmaceutical development.

5. Conclusions

The increasing global demand for pharmaceuticals has highlighted the importance of compounds like α- and β-amyrins, which have demonstrated a wide range of therapeutic benefits. These compounds showed promise in treating various conditions, including anti-inflammatory, anti-diabetic, anti-atherosclerotic, antinociceptive, anti-gout, and neuroprotective effects. They also exhibited potential in addressing serious health concerns such as Parkinson's disease, cancer, bacterial infections, and HIV, all while not inducing cytotoxicity. These effects have been thoroughly tested at the in vivo, in vitro, and clinical levels. This study reaffirmed the value of the previous research that led to the development of a highly efficient method for extracting α- and β-amyrins, yielding a remarkable 10.75 g/kg of raw material. The compounds have been accurately identified and verified using advanced techniques like NMR, GC-MS, and ESI-MS, ensuring the precision of the findings. This study serveed as a valuable reference for further research into utilizing α- and β-amyrins as raw materials for pharmaceutical production, providing a foundation for the development of effective treatments for various diseases.

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