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Apocynin: Bridging Traditional Wisdom and Modern Medicine

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Abstract

Herbal medicines play a significant role in human healthcare system. These botanical medicine or phytotherapy contains a tremendous bioactive compounds or secondary metabolites with many therapeutic effects. In recent days, researchers are showing more interest on these natural compounds for pharmaceutical preparations which offers diverse treatment options. Apocynin, an important secondary metabolite exhibits various medicinal properties and used from olden days to treat several ailments.

This review focused on the pharmacological and biological activities of apocynin and its recent therapeutic advances and mechanistic insights against several diseases.

Keywords: Apocynin; Picrorhiza Kurroa; Apocynum Cannabinum; NADPH Inhibitor

Abbreviations

WHO: World Health Organization; DMSO: Dimethyl Sulfoxide, DMF: Dimethylformamide; BPD: Bronchopulmonary Dysplasia; ALA: Amebic Liver Abscess; ROS: Reactive Oxygen Species; CFA-induced RA: Complete Freund's Adjuvant Induced Rheumatoid Arthritis; SHR: Spontaneously Hypertensive Rats; ISO: Isoproterenol; AOPP: Advanced Oxidation Protein Product; NO: Nitric Oxide; SOD: Superoxide Dismutase; CAT: Catalase; ACR: Acrylamide; APO: Apocynin; UMB: Umbelliferone; MDA: Malonaldehyde; MTX: Methotrexate; KIM-1: Kidney injury molecule 1; NADPH: Nicotinamide Adenine Dinucleotide Phosphate; EETs: epoxyeicosatrienoic Acids; SEH: Soluble Epoxide Hydrolase; CRF: Chronic Renal Failure; GNT: Gentamicin; IBS: Irritable Bowel Syndrome; GI: Gastro Intestinal; SAP: Severe Acute Pancreatitis; DPI: Diphenyleneiodonium; LPS: lipopolysaccharide; BPD: Bronchopulmonary Dysplasia; BLC: Bleomycin; TOS: Total Oxidant Status; OSI: Oxidative Stress Index; GSH: Glutathione; PV: Parvalbumin; GABA: γ-Aminobutyric Acid; TBI: Traumatic Brain Injury; QUIN: Quinolinic Acid; Aβ: Amyloid Beta.

Introduction

Medicinal plants are vital source of food and nutrition for humans from ancient days. These plants are widely used in the traditional medicines to treat various human ailments such as diabetes, ulcers, cancer, heart disorders, etc., [1]. Use of these plant based therapy has been woven into the fabric of healthcare worldwide, from ancient herbalists to contemporary practitioners. Herbal medicine has its origin in the ancient cultures of the Indian, Chinese, Native Americans and Egyptians among others. The usage of plants for medicinal reasons has been documented in texts such as the Chinese herbal classic and the Ebers papyrus. These customs have been handed down through the ages, offering a wealth of information on the therapeutic qualities of the plants.

Medicinal plants and its many parts, including their leaves, stems, and roots can effectively treat illness and aid in the development of new medications. Naturally, Plants contains alkaloids, polyphenols, anthocyanins, saponins, glycosides, terpenoids, polysaccharides, phenols, flavonoids, coumarins, and peptides to treat the variety of illness [2]. These phytochemicals possess a strong physiological actions and wide range of pharmacological characteristics that have been shown to be advantageous to humans including antimicrobial, anticancer, anti-inflammatory, antidiabetic, and hepatoprotective actions and etc.,. The World Health Organization (WHO) estimates that 60% of people worldwide use herbal medicine, and that in developing nations, 80% of people rely exclusively on it for their basic medical requirements [3]. In recent days, studying various plant species to find their potential medicinal uses has gained more attention. Plant based medicines or phytotherapeutics are highly preferred over synthetic derivatives because of their widespread viability, affordability, supposed safety, and a biological friendliness. Combining synthetic medication with active metabolites is one of the latest developments in the pharmaceutical industry. Therefore, it is essential to determine the rich heritage of traditional medicine is crucial.

The objective of this review is to provide an updated understanding of the biological and therapeutic potentials of the phytochemical Apocynin. Using these types of naturally occurring herbal medicines, scientists hope to create a high–specificity drugs with fewer side effects.

Phytochemistry and Pharmacognosy of Apocynin

Apocynin, a natural acetophenone 1-(4-hydroxy-3-methoxyphenyl) ethanone also called acetovanillone, which is similar to Vanillin in structure. It is a potent active metabolite, isolated from the roots of Apocynum cannabinum (Apocynaceae) and Picrorhiza kurroa (Scrophulariaceae). It forms needles upon crystallization from water with a melting point of 115o C. This secondary metabolite is solid with the molecular formula and weight C9H10O3 and 166.1 respectively [4]. It possess a light vanilla odour and soluble in hot water, chloroform, benzene, alcohol, Dimethyl sulfoxide (DMSO) and Dimethylformamide (DMF) [5]. Apocynin exhibits various pharmacological properties such as anti-inflammatory, antioxidant, cardiotonic, anti-asthmatic, NADPH inhibitor, immunomodulatory, neuroprotective, nephroprotective, anti-platelet and many more actions [6] Figure 1.

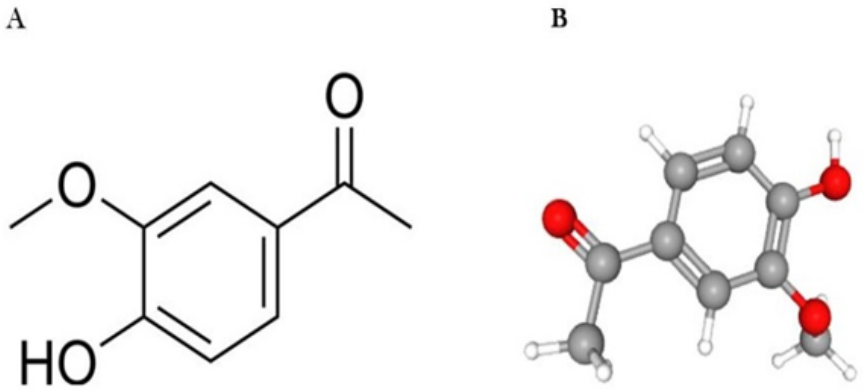

Figure 1: Molecular structure of Apocynin.
A: 2-Dimensional Structure of Apocynin; B: 3-Dimensional Structure of Apocynin

Ethnopharmacological Uses of Apocynin

Apocynin is an active compound from the roots of Picrorrhiza kurroa and Apocynum cannabinum possess strong proven records of numerous biological activities which have been traditionally used in various cultures for medicinal purposes. Both Apocynum cannabinum and Picrorrhiza kurroa used in the Chinese traditional medicine as diuretics, diarrhoea and dysentery. Where as in North America East Asian countries it is used as anti-aging and sedatives [7]. Picrorhiza kurroa root in which apocynin is abundantly seen is widely used for snakebite and scorpion sting in Kashmir. Regional peoples in Himalayas used this root to treat fever, respiratory disorders and allergies. Kutji used in newborns to cure stomach aches along with the mother's milk. In Indian and unani system of medicines, it is the foremost ingredient in Arogyavardhini, an important preparation to treat kidney and liver disorders. It is widely used for cough, fever, indigestion, liver disease, skin disorders, jaundice, metabolic disorders, in Nepal. In Pakistan, kutki used to treat blood and skin disorders [8].

Pharmacological and Therapeutic Roles of Apocynin

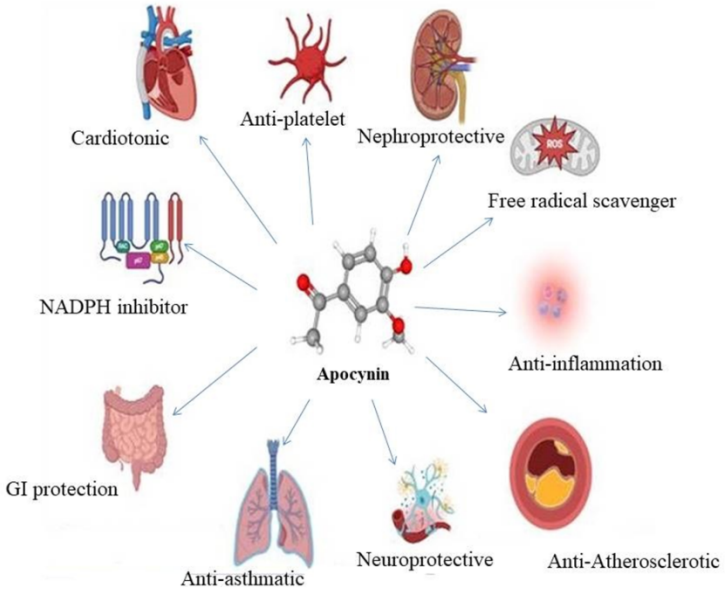

Figure 2: Biological activities of Apocynin.

Apocynin and Inflammation

Inflammation is a vital biological response and a body's defense mechanism, against harmful stimuli and aids in protection from further damage. Though it is a immunological response, chronic inflammation induces the release of inflammatory mediators, which is the important pathophysiological factor for many disorders like asthma, atherosclerosis, hypertension, diabetes, cancer, etc., [9]. Several studies reported the anti-inflammatory actions of the phytochemicals which involve in promote the healing and restores the normal tissue function, inhibits the production of proinflammatory cytokines, modulates inflammatory signaling pathways. Cross AL, et al. [10] reported the anti-inflammatory action of APPA (Apocynin and Paeonol) by inhibiting the neutrophil degranulation, cytokine stimulated gene expression, TNFα and GM-CSF cell signaling, chemokine and IL-6 expressions that are associated with the inflammation. This investigation clarifies that APPA reduces the inflammation and be a possible therapeutic inflammatory disorder like rheumatoid arthritis, where neutrophils and TNFα signaling play a significant role in pathophysiology [10]. Tayman C, et al. [11] investigated the therapeutic effect of Apocynin against hyperoxia and inflammation induced lung injury in rat pups. Apocynin, treatment reduced free radical damage, blocked inflammation, reduced the inflammatory cell infiltration and proinflammatory cytokines, supressed NLRP3 inflammasone activation including Nrf2, confirmed Apocynin a potential treatment option for Bronchopulmonary dysplasia(BPD) [11]. In a study conducted by Higuera-Martinez G, et al. [12], the anti-inflammatory action exhibited by significant reduction of Amebic liver abscess (ALA), size of the inflammatory foci, neutrophils count, and the activity of NADPH oxidase. In vitro, this apocynin damages amoebae and decrease ALA progression by targeting the inflammatory pathway and reactive oxygen species (ROS). This substantiates not only the anti-inflammatory properties but also the antioxidant actions of apocynin [12]. Aman RM, et al. [13] investigated the aniinflammatory actions of apocynin by nanophyto mediated topical gel formulation called APO-loaded Compritol® 888 ATO (Lipid)/chitosan (polymer) hybrid nanoparticles (APO-loaded CPT/CS hybrid NPs). The APO(Apocynin)-hybrid NPs based gel showed potential as a topical nanostructured system for treating rheumatoid arthritis in Complete Freund's Adjuvant induced rheumatoid arthritis (CFA-induced RA) rats [13].

All these studies supports the promising approach of the bioactive compound Apocynin that could break new ground in phytopharmaceutical therapeutic involvement in inflammatory –dependent ailments.

Apocynin and Oxidative Stress

Oxidative stress plays a vital role in mediating various diseases like cancer, diabetes, lung disorders, cardiovascular disease; neuroinflammatory disease etc., Antioxidants is the imbalance between the radical engendering and radical

scavenging system. Antioxidants are able to prevent or reduce other molecules from oxidizing. Antioxidant therapy received attention in the management of many disorders [14]. Chen QZ, et al. [15] investigated the potential of apocynin, a NADPH inhibitor, to reduce arterial stiffness in salt-sensitive hypertensive rats. Results showed that tail blood pressure was higher in DSH (Deoxycorticosterone acetate salt hypertensive) rats, leads to significant remodelling in large arteries. Treatment with apocynin prevented ROS increase and collagen deposition, reduced arterial stiffness, and prevented carotid artery wall thickening. Also, this study suggested the antioxidant therapy could be a potential treatment for large arterial stiffness and thereby related cardiovascular disorders [15]. Therapeutic effect of apocynin was evaluated by Sun Y, et al. [16], based on its antioxidant activity and ability to suppress apoptosis and inflammation after spinal cord injury. Experimental rats with spinal cord injury were treated with apocynin showed decreased oxidative damage, alleviated neuronal apoptosis, inhibited inflammatory response, and promoted locomotor function. This confirms the therapeutic efficacy of Apocynin in Spinal cord injury repair, likely through the inhibition of apoptosis and inflammatory response, promoting nerve function restoration [16]. In a study conducted by Kurosawa T, et al. [17], in vitro effects of apocynin were demonstrated against high glucose induced oxidative stress. Tenocytes from normal Sprague- Dawley rats were cultured in various glucose conditions, with apocynin added as seeding.The tenocytes were divided into four groups control, high glucose with apocynin (HG apo+), and high glucose without apocynin (HG apo–). In vitro, NOX1 and IL-6 mRNA expression was higher in HG groups, and cell proliferation was higher in Regular glucose (RG apo+) and (HG apo+ groups). Thorugh NOX Inhibition, apocynin decreased the generation of ROS and cell death in high glucose conditions. Thus, apocynin may be used as a prodrug option in the management of diabetic tendinopathy [17]. Apocynin, a strong antioxidant, is being evaluated for its effect on CCL4-administered hepatic dysfunction in rats. Female long evans rats treated with carbon tetrachloride and found that apocynin significantly reduced enzymatic parameters such as AST, ALT, ALP activities. Majorly, apocynin reduced the oxidative stress markers, catalase and superoxide dismutase and also prevented inflammation and tissue fibrosis in rats, as confirmed by histological staining of liver tissue sections. Thus, these clinical findings highlight the potential of apocynin in reducing the oxidative stress [18].

Apocynin and Cardiovascular Disorders

Globally, cardiovascular disorders remain a major health concern. Heart failure, hypertension, and coronary artery disease are still common conditions that are frequently made worse by lifestyle choices including smoking, poor eating, and inactivity. Due to the pandemic, there have been more complaints of heart problems among COVID-19 patients, and usual care for chronic illnesses has been disrupted. Mohammad A, et al. [19], investigated the role of an NADPH oxidase inhibitor (apocynin) in protecting the heart from ischemia and perfusion injury. Hearts from Wistar rats were perfused with a modified Langendorff preparation, and their left ventricular contractility and cardiovascular hemodynamics were evaluated. Apocynin was infused before, during, or at reperfusion, and its effects on pro-inflammatory cytokines and anti-inflammatory cytokines were evaluated. The study found that apocynin infusion improved cardiac hemodynamics and coronary vascular dynamics, decreasing infarct size and inflammatory cytokine levels, and increasing anti-inflammatory and antioxidant levels [19]. Gimenes R, et al. [20], conducted a study and examined the impact of apocynin, on cardiac remodeling in diabetic rats, highlighting its potential role in reducing reactive oxygen species generation. Six-month-old male Wistar rats were divided into four groups: control + apocynin: control, diabetes, and diabetes + apocynin. Diabetes was induced by streptozotocin, and apocynin was initiated and maintained for 8 weeks. Left ventricular histological sections were used to analyze interstitial collagen fraction and NADPH oxidase activity. Results showed that body weight was lower and glycemia higher in diabetic animals, and echocardiogram showed increased left atrial diameter, LV diastolic diameter, and LV mass. Myocardial functional evaluation showed impaired contractile and relaxation function in both diabetic groups [20]. In a study, impact of chronic treatment with apocynin on hypertensive rats' vascular endothelium, focusing on its effects on acetylcholine, sodium nitroprusside, and phenylephrine action was investigated. Results showed that apocynin significantly reduced arterial pressure in Spontaneously Hypertensive Rats (SHR) and improved the impaired ACh hypotensive effect. The study also found that apocynin normalized overexpression of NOX2 and its subunit p47phox in the aortas of treated SHR, suggesting that apocynin increases NO bioavailability and restores proper vascular endothelium function [21]. Isoproterenol (ISO)-induced cardiac damage in male Wistar rats were treated with apocynin for two weeks, and their blood plasma and heart tissues were analyzed for oxidative stress-related parameters such as Malondialdehyde, Advanced oxidation protein product (AOPP), Nitric oxide (NO), Catalase (CAT), Superoxide dismutase (SOD). The results showed that apocynin effectively normalized serum transferases and CK-MB activities, suppressed ISO-induced elevations of MDA, NO, and AOPP levels, and restored reduced SOD and catalase activities. Histological analysis showed amelioration of mononuclear cell adherence and fibrosis in the cardiac tissue [22]. A study conducted by Qiu J, et al. [23] to examine the therapeutic potential of apocynin, in which 30 Japanese rabbits grouped in three groups, showed that alloxan-induced

diabetes led to increased interventricular septal thickness, left ventricular posterior wall thickness, increased LV cardiomyocyte cross-sectional area, and greater interstitial fibrosis. The diabetic group also had higher levels of NO, myeloperoxidase, malonaldehyde, and protein expression. Apocynin treatment prevented these structural, histological, and biochemical changes and increased superoxide dismutase levels [23].

All these recent findings evidence the apocynin may have potential applications in various diseases, including cardiovascular diseases.

Apocynin and Nephrotic Disorders

Nephrotic disorders are characterized by a group of clinical features resulting from glomeruli damage in the kidneys which involve immune mediated injury, metabolic disturbances and structural variations in the glomeruli. This in turn affects RAAS system contributes to hypertension and edema, which causes damage to the cardiovascular system, followed by liver and cause dyslipidemia. Ageena SA, et al. [24] investigated the Acrylamide (ACR)-induced acute kidney injured rats, to study the combination of the phytochemicals apocynin (APO) and/or umbelliferone (UMB). The results show that APO, UMB, and their combination significantly reduced kidney function biomarkers, prevented tissue damage, and decreased inflammatory cytokines and malonaldehyde (MDA). Also, the phytochemicals combination decreased the expression of NLRP-3, ASC, GSDMD, caspase-1, and IL-1β, 1β in the kidneys of rats given ACR, while upregulating Nrf-2 and HO-1 at the molecular level [24]. Hassanein EHM, et al. [25], assessed the renoprotective effects of apocynin (APC) against methotrexate (MTX)-induced nephrotoxicity in rats, in which APC significantly decreased urea, creatinine, and Kidney injury molecule 1(KIM-1) levels, improved kidney histological alterations, and restored oxidant/antioxidant balance. It also reduced iNOS, NO, p-NF-κB-p65, Ace-NF-κB-p65, TLR4, p-p38-MAPK, p-JAK1, and p-STAT-3 expressions. APC protected MTX-induced cytotoxicity in NRK-52E cells, and inhibited the JAK/STAT3 pathway. The findings suggest APC could be a potential candidate for MTX-induced renal damage [25]. Another study explained the medicinal importance of apocynin, a nicotinamide-adenine dinucleotide phosphate (NADPH) inhibitor, shown to have cardio-protective effects. in which 94 participants and 5/6 nephrectomized rats showed that apocynin reduced serum levels of epoxyeicosatrienoic acids (EETs) and increased the ratio of left ventricular weight/body weight, left ventricular posterior wall thickness, and cardiac interstitial fibrosis in renocardiac syndrome participants. Additionally, apocynin increased reduced serum levels of EETs and decreased soluble Epoxide Hydrolase (sEH) expression in the heart during cardiac remodeling in chronic renal failure (CRF) [26]. Abdelrahman R [27] studied the renoprotective effects of apocynin against the adverse effects of aminoglycosides. The experimental rats were induced nephrotoxicity using Gentamicin (GNT), an aminoglycosides. The rats were divided into three groups: control, GNT (100 mg/kg), and GNT plus APO (10 mg/kg). GNT-induced nephrotoxicity increased kidney weight, urine volume, and protein levels. APO ameliorated this by improving tissue morphology and decreasing these effects. APO also increased renal SOD activity and CCr levels. These findings suggest APO's anti-inflammatory, antiapoptotic, and antioxidant effects can mitigate GNT-induced nephrotoxicity [27].

Apocynin and Git Disorders

Gastrointestinal disorders encompasses a wide range of conditions affecting the digestive system.it includes GERD, Irritable Bowel syndrome(IBS), Peptic ulcer disease, Inflammatory bowel disease, gastroenteritis, celiac and diverticulis disease, etc. Kouki A, et al. [28] investigated the Gastro Intestinal (GI) preventive effect of apocynin, a natural antioxidant molecule, on acetic acid-induced ulcerative colitis in rats. Results showed that apocynin has a high free radical scavenging capacity and potent iron chelating ability. Oral pretreatment suppressed pro-oxidant markers in colonic homogenates and preserved colonic cytoarchitecture from acetic acid-induced damage. This suggests apocynin may have a promising beneficial effect in preventing ulcerative colitis [28]. A study on rats showed that apocynin, given orally one hour before ethanol administration, provided 93.5% gastroprotection against ethanol-induced gastric ulceration. Apocynin increased gastric mucin content, reduced gastric juice volume and acidity, and ameliorated ethanol-induced oxidative stress. It also decreased pro-inflammatory response and caspase-3 tissue levels. Apocynin reversed up-regulation of NADPH oxidase-1 and NOX-4, which was partially involved in the pathogenesis of ethanol-induced gastric ulceration. This study is the first to show apocynin's potential as a gastroprotective agent [29]. In a study conducted, Apocynin, a nicotinamide adenine dinucleotide phosphate (NADPH) oxidase inhibitor, shown to decrease inflammatory and oxidative stress parameters in rats with severe acute pancreatitis (SAP). The study investigated the protective effects of apocynin on intestinal mucosal injury in a rat model of SAP. Experimental rats were divided into four groups, and apocynin was administered 30 min before SAP induction. The results showed that apocynin attenuated various intestinal pathological injuries, MDA content and inflammatory cytokines. This suggests that apocynin may be a potential therapeutic method for treating intestinal injury in SAP [30]. Another study evidenced the GI protective role in which colitis were induced experimentally in a BALB/c mouse, and apocynin (400 mg/kg) and sulfasalazine (150 mg/kg) were administered for 7 days. Apocynin significantly

alleviated weight reduction induced by (Dextran sulphate sodium) DSS treatment and showed anti-inflammatory efficacy. Histopathologic examination revealed reduced inflammatory foci and erosions in the apocynin treated group. Apocynin's unique action compared to sulfasalazine suggests it could be a new therapeutic molecule for IBD treatment [31]. Mansoury, et al. [32] investigated the potential of apocynin (APO) as a potential therapeutic agent against Methotrexate (MTX)-induced mucositis. APO was administered orally to 32 rats, reducing oxidative stress, inflammation, and apoptosis. The results showed that APO protected the duodenal mucosa structure, mitigated oxidative stress, reduced proinflammatory cytokines, and upregulated anti-apoptotic Bcl2 mRNA. This suggests APO could be a potential therapeutic agent for MTX-induced mucositis [32].

Apocynin and Respiratory Disorders

Lungs and Respiratory passages affected with various factors like infective agents, environmental factors, genetic predisposition, life style and immunological factors influence the development and exacerbation of inflammation in respiratory path. Several respiratory disorders such as COPD, Emphysema, asthma, Pneumonia, pulmonary fibrosis and embolism, Tuberculosis, Interstitial lung disease, cystic fibrosis ,etc. Kouki A, et al. [33] investigated the effects of two NADPH oxidase inhibitors, apocynin and diphenyleneiodonium (DPI), on lipopolysaccharide (LPS)-induced lung inflammation in rats. Results showed that apocynin and DPI attenuated lung morphological and histological alterations, reduced edema, and decreased lung permeability. They also inhibited LPS-induced NADPH oxidase activity, restored superoxide dismutase and catalase activity, and reduced LPS-induced protein and lipid oxidation [33]. Another study investigated the effectiveness of apocynin (APO), an anti-inflammatory, antioxidant, and antiapoptotic drug, in preventing neonatal hyperoxic lung injury. The study involved 40 neonatal rats divided into control, APO, Bronchopulmonary dysplasia (BPD), and BPD+APO groups. The rats were given intraperitoneal APO, while the control and BPD rats received saline. The results showed that BPD and BPD+APO groups had higher mean histopathological injury and alveolar macrophage scores, lower TUNEL positive cells, and higher levels of malondialdehyde, total oxidant status, TNF-α, and IL-1β. The BPD group also had lower antioxidant enzyme activity. Thus apocynin, exhibits the anti-inflammatory, antioxidant, and antiapoptotic properties used in the prevention of neonatal hyperoxic lung damage [34]. A study conducted by Kilic T, et al. [35] revealed the preventive and therapeutic effects of apocynin (APO) on bleomycin (BLC)-induced lung injury in rats. Rats were divided into groups, with APO administered intraperitoneally for 29 days, BLC-1 and BLC-2 groups given a single injection, and BLC+APO-treatment group given 20 mg/kg. Histopathological assessments showed significant BLC-induced changes, including decreased GSH, CAT, and GPX, increased MDA, Total oxidant status (TOS), and oxidative stress index (OSI), and increased cellular account and proinflammatory cytokines in BAL (Bronchoalveolar lavage) fluid. Also, it reversed the Myeloperoxisdase(MPO) activity and all biochemical markers and cytokine changes induced by BLC [35].

Apocynin and Neuroinflammatory Disorders

Gradual loss of neurons and brain function causes the neurodegenerative disorders, are often exacerbated by chronic inflammation such as Alzheimers disease. Uehara T, et al. [36] derived new compounds from apocynin and tandospirone to test their antioxidant properties. These compounds, along with olanzapine and clozapine, decreased intracellular reactive oxygen species (ROS) formation and reduced glutathione (GSH) levels and parvalbumin (PV)-positive γ-aminobutyric acid (GABA) interneurons in rats exposed to MK-801 during puberty. These findings suggest that these compounds may provide a novel therapeutic approach for schizophrenia and its spectrum disorders, potentially addressing the pathophysiology of the illness [36]. Feng Y, et al. [37] investigated the neuroprotective effect of apocynin in Traumatic Brain Injury (TBI) rats .The rats were injected with apocynin after the injury, and their brain water content and histology were analyzed. The treatment significantly attenuated TBI-induced impairment, brain edema, and neuronal damage. The protective effects of apocynin may be related to modulating neuronal autophagy and the TLR4/NF-κB signaling pathway [37]. Cruz-Alvarez S, et al. [38] evaluated the effect of Apocynin (APO) administration on glutathione (GSH) levels, enzyme activity, and Nrf2 mRNA levels in rats injected with quinolinic acid (QUIN). Results showed that APO treatment prevented QUIN-induced striatological damage, increased GSH and Nrf2 mRNA levels, and increased gamma-glutamylcysteine ligase, glutathione-S-transferase, and glutathione peroxidase activities. However, APO treatment prevented QUIN-induced decrease in GSH and Nrf2 levels. This indicates the apocynin ability to raise GSH levels and modulates the Nrf2 mRNA levels [38]. Pan L, et al. [39] explored the protective roles of apocynin, against cerebral infarction. After middle cerebral artery occlusion surgery, rats treated with apocynin showed improved neurological function, increased forelimb placement test scores, and suppressed balance beam walk latency. Apocynin also reduced cerebral infarction volume and water content, suppressed neuronal apoptosis, and suppressed the Tlr4/nuclear factor-k-gene binding signalling pathway [39]. Joseph E, et al. [40] used the scopolamine model, which replicates the increase in amyloid beta and oxidative stress in vivo, was used to analyze the

neuroprotective effects of apocynin and galantamine. Results showed that scopolamine induced cognitive impairment, increased amyloid beta (Aβ) and superoxide anion levels, and overexpressed NADPH oxidase 2 and NFkB genes. However, both apocynin and galantamine reduced Aβ production and superoxide anion production through different pathways [40].

Conclusion

Apocynin posess a tremendous therapeutic potentials through its role in inhibiting the enzymes NADPH oxidase,which involved in the production of reactive oxygen species (ROS) and various inflammatory mediators. This implies the apocynin to approach a greater significance to check the potential improvement against cancer, renal and neuroinflammatory disease, atherosclerosis. Apocynin's role in molecular signaling primarily revolves around its inhibition of NADPH oxidase and subsequent reduction and may target pro-inflammatory molecules such MAPK, iNOS, NF-kB, nitrotyrosine, PARP, TNF-α, ICAM-1, p-selectin, CD31, P38, MPO, MCP-1, and IL-6 that contribute to chronic inflammation. These research findings capable of addressing the underlying mechanisms of disease rather than alleviating the symptoms.

Thus, the potential of apocynin as a therapeutic agent warrants further investigation and may contribute significantly to the advancement of various health conditions in the near future.

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