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REVIEW ARTICLE

RECENT ADVANCES IN PHARMACOLOGICAL PROPERTIES OF INULIN: A MINI REVIEW

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ABSTRACT

Inulin is a polymer primarily composed of fructose units, and glucose unit at the end. It is neither digested nor absorbed in the stomach, thus staying in the bowel. Although it gets metabolized by bacteria in the colon to a gel that helps certain beneficial gut microflora grow, it could be classified as a prebiotic. Multiple research studies have been conducted to uncover its pharmacological use in various chronic disorders, but compiled information is lacking in the current literature. The recent advances in its pharmacological effects such as neuroprotective effects, anti-diabetic, hepatotoxicity, anti-oxidant, and anti-inflammatory were discussed in this article. It showed promising pharmacological properties and can be explored further for developing formulations against the neuro-disorders, diabetes, liver and inflammatory bowel diseases.

INTRODUCTION

In 1804, German scientist Valentin Rose discovered inulin by extracting it from Inula helenium roots. Inulin is a polymer primarily composed of fructose units, and glucose unit at the end [1]. It is commonly found in herbs, fruits and vegetables, including garlic, bananas, onions, wheat, leeks, chicory, Jerusalem artichokes, asparagus, and artichokes [2]. It is utilized as an energy reserve and regulates cold resistance in these plants and found to be water-soluble therefore osmotically active [3]. Certain plants protect themselves from cold and drought during the winter period by changing their osmotic potential. This is achieved by altering the degree of polymerization of inulin molecules through hydrolysis without

changing the total carbohydrate content [4]. It is neither digested nor absorbed in the stomach, thus staying in the bowel. Although it gets metabolized by bacteria in the colon to a gel that helps certain beneficial gut microflora grow, it could be classified as a prebiotic [5]. A significant quantity of carbon dioxide, hydrogen, and/or methane is released, which could be responsible for bloating and flatulence. It is commonly taken by mouth for weight loss, constipation, diabetes, controlling hyperlipidemia, preventing traveller's diarrhoea, increasing calcium absorption in adolescents, and several different conditions, but there is a lack of research findings to aid most of these uses [6]. The clinical trials have revealed that it causes gastrointestinal adverse effects like flatulence and bloating, which advocates its use in moderate quantities [7]. Although, inulin is being used to find out the glomerular filtration rate, it is not being reabsorbed or secreted after introduction into tubules due to its resistance to enzymes and its high molecular weight [8].

Numerous research studies have been conducted to uncover its pharmacological use in various chronic disorders, but compiled information is lacking in the current literature. Hence, it was decided to compile the recent development in sources, process of extraction and pharmacological applications which will help researchers for further research. This review provides a deep insight about inulin's sources, chemistry & SAR, extraction process, role of inulin in various therapeutic application and its utilization as a functional ingredient in the development of novel products.

SOURCES

Inulin is found in over 36,000 plant species, such as chicory, agave, Jerusalem artichoke, wheat, asparagus, onion, garlic and banana, these plants have diverse therapeutic uses, inulin could be responsible for these actions [Table 1]. The dietary intake of the prehistoric hunter-gatherer in the Chihuahuan Desert is predicted to comprise 135 grams of inulin-type fructans daily [9].

Table 1: Sources of inulin

Sr No.	Source	Plant part	Inulin content [g/100g]	Therapeutic use
1.	*Cynara cardunculus* (Artichoke)	Leaves	85	Anti-rheumatic, diuretic, lithontripic, early stages of late-onset diabetes, chronic liver/gall bladder diseases, hepatitis, arteriosclerosis and the jaundice [10].
2.	*Articum lapp. L* (Burdock)	Fruits and Roots	50	Diabetes mellitus, skin inflammation and digestive tract diseases [11].
3.	*Allium sativum* (Garlic)	Rhizome	18-19	Diabetes and its complications [12].
4.	*Cichorium intybus* (Chicory)	Flowers	68	Diabetes mellitus, appetite stimulant, gallstones, gastroenteritis, sinus problems, cuts, and bruises [13].
5.	*Allium cepa* (Onion)	Bulb	25	Antidiabetic effects, bronchitis, pain and swelling after bee or wasp stings, inflammatory disorders, asthma, ulcer wounds dysentery, keloids and scars [14].
6.	*Asparagus officinalis* (Garden asparagus)	Root	2-3	Antidiabetic, remedy for schistosomiasis and tuberculosis [15].
7.	*Jerusalem artichoke* (Artichoke)	Root	53	Antidiabetic and increase the beneficial intestinal microbiota [16].

8.	*Allium porrum* (Leek)	Stem	16	Antidiabetic, gastric ulcer, tuberculosis, anti - hypertiensive and anti - helmenthic, blood clotting disease [17].
9.	*Triticum* (Wheat)	Seed	1-4	Diabetes, Anti -cancer, Strengthens the bones [18].
10.	*Musa* (Banana)	Leaves	0.3-0.7	Antidiabetic, ant -cancer, anti-ulcer. Anti-alzheimer's disease, anti -infection, anti-diarrhea, hemorrhoids, anti - diabetes, and anti - hypertension [19].
11.	*Taraxacum officinale* (Dandelions)	Leaves Roots Fruits	45	Anti-diabetes and anti - cancer, diuretic, choleretic, anti-inflammatory, anti - rheumatic, digestive - stimulant, alterative, and depurative properties. Anti-hypertension, dyspepsia, irritable bowel syndrome, and ovarian androgen excess [20].
12.	*Smallanthus sonchifolius* (Yacon)	Roots Leaves	9.25+/- 0.44	Anti-diabetic [21].
13.	*Hordeum vulgare* (Barley)	Fruit	0.5-1.5	Anti-diabetic [22].

CHEMISTRY

Inulin's structure primarily consists of β-D-fructosyl units connected by (2→1) glycosidic bonds, typically terminating with an α-D-glucosyl group linked via a (1↔2) bond. The fructose chain length varies, generally ranging from 2 to 60 monomers, though it can extend up to 100. Its physicochemical and functional characteristics are influenced by the degree of polymerization (DP) and structural branching. Higher DP inulin serves as a fiber-like prebiotic, offering potential health benefits. However, as DP increases, inulin’s solubility decreases.

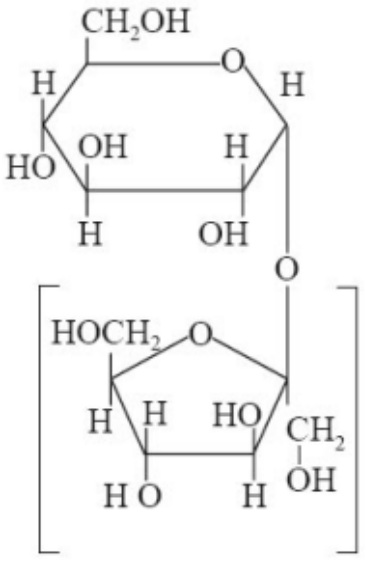

Figure 1: Structure of Inulin

Chemical formula:C12H22O11

Molar mass:342.3 g/mol

Boiling point =563.5°C

Melting point=176-181°C

Density 1.85 g/cm³

pubchem CID: 24763

RECENT ADVANCES IN THERAPEUTIC APPLICATIONS

Antidiabetic effect:

Diabetes is a medical disorder that affects the process of converting food into energy. Inulin has been screened for antidiabetic effect. Inulin and resveratrol together demonstrated renoprotective effects in diabetic rats by reducing oxidative stress and inflammation in kidney tissues, suggesting a low-cost treatment option for diabetic nephropathy [23]. In another study, inulin and Lycium barbarum polysaccharides improved the gut barrier and decreased hyperglycemia in rats by altering the gut microbiota and stimulating TLR2+ intraepithelial γδ T cells in the gut mucosa [24]. Furthermore, inulin-type fructan demonstrated a protective effect against gestational diabetes mice caused by a high-fat/sucrose diet [25]. In experimental animals, inulin fermentable fiber reduces type I diabetes via IL22 and short-chain fatty acids [26]. Recent research has indicated that inulin may prove to be a useful treatment for diabetes.

Antioxidant activity:

Inulin showed anti-oxidant activity in DPPH and ABTS radical scavenging assay [27]. The anti-oxidant activity of inulin is

correlated to its molecular characteristic [28]. Inulin intake results in increase in lactobacilli counts which increase lactic acid synthesis, lactic acid itself has antioxidant activity and thus inulin shows antioxidant activity [29]. In one of the studies, phosphorylated derivatives of long-chain inulin with different substitution degrees were prepared, the findings demonstrated that phosphorylation can improve its physicochemical characteristics and biological activity, including antioxidant effects, indicating its potential as a functional food ingredient and quality enhancer [28]. The effects of inulin supplementation on HFD-induced obesity with hepatic oxidative stress and anxiety-related defensive behavior were evaluated. Inulin supplementation restores the hepatic redox balance followed by a decrease in CAT activity and amounts of carbonylated protein [30].

Anti-inflammatory effect

Inulin is a prebiotic and polysaccharide has anti-inflammatory activity. A recent study highlighted that inulin may assist in managing recurrent inflammatory bowel disease symptoms by modulating gut microbiota, reducing inflammation, and alleviating endoplasmic reticulum (ER) stress [31]. Olsalazine-based MOF nanoneedle/inulin gel hybrid (Cu_2(Olsa)/Gel) reshaped intestinal homeostasis in inflammatory bowel disease. Cu_2(Olsa)/Gel displayed anti-oxidative and anti-inflammatory effect and enhanced bio-adhesion and colon retention [32]. Inulin administration in mice with type 2 diabetes (T2DM) Inulin administration reduced diabetes-induced chronic inflammation and mitigated renal damage [33].

Hepatoprotective property

Several research articles have proven inulin's hepatoprotective activity in their study. Catechin grafted inulin was investigated against carbon tetrachloride (CCl_4)-induced acute liver injury, it showed higher *in-vitro* antioxidant activity and stronger hepatoprotective effect *in-vivo* than inulin [34]. Inulin was found to be hepatoprotective against methotrexate induced hepatotoxicity might be mediated via the modulations of apoptotic and oxidative stress factors [35]. Inulin-type fructan demonstrated significant liver-protective effects in vivo, likely due to its antioxidant and immune-regulating properties [35]. Deoxynivalenol is a *Fusarium* mycotoxin which induced oxidative stress, cytotoxicity and genotoxicity. Inulin nanoparticles alleviated DON toxicity [36]. Inulin helps prevent non-alcoholic fatty liver disease by regulating gut microbiota and inhibiting the LPS-TLR4-Mψ-NF-κB-NLRP3 inflammatory pathway through the gut-liver axis [37].

Neuroprotective effect

The recent research showed promising neuroprotective effects of inulin, in one of the studies, evening administration of

inulin is more effective in reducing inflammation and enhancing amino acid metabolism and reduced CUMS-induced anxiety and depression. This study suggests a potential connection between the microbiota-gut-brain axis and chrono-nutrition, highlighting that optimal timing of administration enhances intervention effectiveness [38]. Inulin reduces blood-brain barrier permeability and mitigates behavioral disorders by regulating the TLR4/MYD88/NF-κB pathway in chronically stressed mice. Additionally, it modifies gut microbiota to relieve post-stroke depressive-like behavior through the IGF-1-mediated MAPK signaling pathway [40]. Prolonged preventive supplementation with inulin reduced anxiety, cognitive impairments, and dysbiosis in mice subjected to chronic unpredictable stress [41].

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