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Mechanism based Antianxiety activity of Polysaccharides obtained from different medicinal plants A Review on Current evidences

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Abstract

Anxiety is major disorder affecting world population about estimated 33% population in the world are suffering from psychosis, mental and neurological diseases. Polysaccharides obtained from many medicinal plants can be used in treatment of various conditions like antioxidant, antidepressant, hyperglycemia, anti-inflammatory, heamatinics, immune modulator activities and many more. In present review article the study of polysaccharides from different medicinal plants with their anxiolytic effects was reviewed. Based on review this study shows potentials of different homo and hetero polysaccharides extracted from different medicinal plants, responsible for anxiolytic activity in preclinical models. Polysaccharides are derived from a variety of sources, including plants, microorganisms, algae, and animals. Their unique physicochemical properties make them amenable to physical and chemical modifications, which can enhance their characteristics. This versatility underpins their growing applications in biomedical and pharmaceutical fields. In this review, we will explore the current advancement in polysaccharide applications as anxiolytics.

Key words : Anxiolytics, Polysaccharides, Preclinical models, growing applications.

Anxiety disorders encompass a range of mental health conditions characterized by excessive fear and apprehension that often do not match the actual situation[1]. Common types include generalized anxiety disorder, specific phobias, and social anxiety disorder. Effective treatment typically combines medication with psychotherapy[1]. Psychological symptoms may include: Feeling panic, fear, dread and uneasiness, Feeling on edge or irritable, Uncontrollable obsessive thoughts, difficulty in concentrating while Physical symptoms may include: Restlessness, Heart palpitations, Shortness of breath, Muscle tension, Cold or sweaty hands, Dry mouth, Nausea, Numbness or tingling in your hands or feet, difficulty falling asleep or staying asleep (insomnia).As socio-economic development progresses and pressures on individuals rise, there has been a significant increase in the number of people experiencing

anxiety. This trend poses serious challenges for both society and families. Due to its association with self-harm, suicidal thoughts, and violent behaviors, anxiety is recognized as the mental health condition with the highest suicide rate globally after depression.

Additionally, it can significantly impact the patient's digestive, immune, and nervous systems, leading to further health complications[4]. The pathogenesis of anxiety were studied with emotional processing in rodents (Rogan & LeDoux et.al. 1996) and in humans with brain lesions[1] have identified the amygdala as critical to fear responses. Sensory information enters the lateral amygdala, from which processed information is passed to the central nucleus, the major output nucleus of the amygdala. The central nucleus projects, in turn, to multiple brain systems involved in the physiologic and behavioral responses to fear[7]. Projections to different regions of the hypothalamus activate the sympathetic nervous system and induce the release of stress hormones, such as Corticotropin releasing hormone (CRH). The production of CRH in the paraventricular nucleus of the hypothalamus activates a cascade leading to release of glucocorticoids from the adrenal cortex. The complete patho-physiology of anxiety was mentioned in fig. 1.

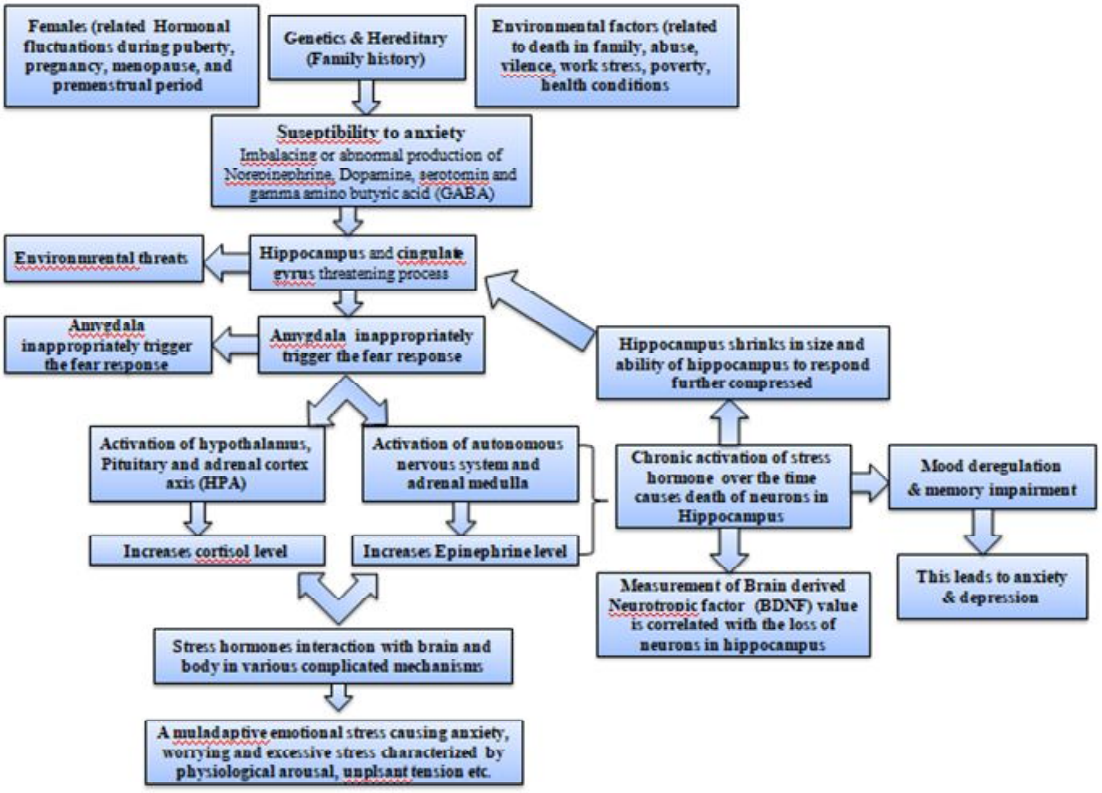

Fig. 1. Pathogenesis and effects of Anxiety in Detail

First-line treatment of anxiety typically include selective serotonin reuptake inhibitors (SSRIs) and serotonin-norepinephrine reuptake inhibitors (SNRIs). Benzodiazepines are generally discouraged for regular use[10]. Additional options may involve pregabalin, tricyclic antidepressants, buspirone, moclobemide, and other alternatives. While these medications can alleviate symptoms of anxiety, there is currently no definitive cure. Antipsychotic drugs are restricted to acting on a single site or type of target, which contributes to the challenges of managing anxiety, including low remission rates, high recurrence rates, and significant side effects for patients. Only 12.7% of individuals receive minimally adequate treatment[11]. Although Western clinical antianxiety drugs in allopathic have clear targets and offer rapid effects, they often exhibit low efficacy, a limited mechanism of action, and considerable adverse effects. Given the complexity of anxiety's underlying mechanisms, the development of new multi-target drugs is crucial for improving treatment outcomes. Consequently, the pursuit of an anxiolytic medication that offers high efficacy, sustained effectiveness, and minimal side effects has emerged as a significant area of research. Polysaccharides derived from natural sources have garnered considerable interest due to their diverse pharmacological properties and reduced adverse effects. Polysaccharides are biologically active macromolecules composed of monosaccharides linked by glycosidic bonds, formed from polyhydroxy polymers and their derivatives. They are prevalent in natural products from higher plants, animals, microorganisms, and algae. Numerous studies indicate that polysaccharides possess anti-inflammatory, antioxidant, antiviral, immune-regulating, hypoglycemic, and hypolipidemic properties, as well as the ability to modulate gut microbiota[12,17]. Additionally, research has shown that polysaccharides from natural sources can effectively reduce anxiety, and the mechanisms behind their action have drawn significant interest from scientists. Some researchers have suggested that the mechanisms involved in reducing anxiety are linked to the modulation of brain function and the regulation of biological and immune barriers. Polysaccharides derived from natural products typically target multiple pathways, offering significant therapeutic benefits with fewer side effects. However, there are limited studies exploring the connection between polysaccharides and anxiety. This review highlights recent advancements in research on the anxiolytic effects of polysaccharides, focusing on various mechanisms of intervention. It aims to provide insights for further investigation into the prevention, alleviation, and treatment of anxiety, as well as the development of therapeutic drugs.

Anxiolytic mechanism of natural plant polysaccharides :

Polysaccharides from natural plant sources help alleviate anxiety by modulating the expression of neurotransmitters and their receptors, the HPA axis, neurotrophic factors, neuroinflammation, oxidative stress, tryptophan metabolism, and gut microbiota[14]. Various plant polysaccharides from different sources can produce anxiolytic effects through a range of mechanisms, as summarized in Table-1.

Polysaccharide effects on NE, DA and 5-HT :

The mechanism of action underlying the majority of current anxiolytics is based on

Table-1. Various plant polysaccharides which can produce anxiolytic effects through a range of mechanisms

Plant Name	Polysaccharide Source	Monosaccharides Composition	Validation Model	Parameters Evaluated	Administration Route	Target Mechanism	Effects	Reference
Panax ginseng	Ginseng root	Glucose, Galactose	EPM, FST, TST & OFT	Cortidol,TNF-α, IL-6, IL-1β, BDNF, serotonin (5-HT), dopamine (DA), and GABA.	Oral	HPA axis modulation	Reduced anxietylike behavior	Choi *et al.*, 2016
Rehmannia glutinosa	Rehmannia root	Glucose, Fructose	EPM, OFT & LD	Microbiota composition, ACTH, TNF-α, IL, IL-1β, serotonin (5-HT), dopamine (DA), and gamma-aminobutyric acid (GABA),SOD, CAT, MDA.	Oral	Neuroinflammatorypathways	Decreased anxiety symptoms	Zhang *et al.*, 2019
Lentinula-edodes	Shiitake mushroom	Mannose, Galactose	EPM, OFT & LD	Microbiota composition, ACTH, TNF-α, IL, IL-1β, serotonin (5-HT), dopamine (DA), and gamma-aminobutyric acid (GABA)	Oral	Gut microbiota regulation	Anxiolytic effects through gut modulation	Yang *et al.*, 2021
Ganoderma lucidum	Reishi mushroom	Glucose, Galactose	EPM, OFT & LD	Microbiota composition, ACTH, TNF-α, IL, IL-1β, serotonin (5-HT), dopamine (DA), and gamma-aminobutyric acid (GABA),SOD, CAT, MDA	Oral	Neurotransmitter modulation	Reduced anxiety-like behavior	Chen *et al.*, 2022
Poriacocos	Poria fungus	Glucose, Galactose	EPM, OFT & LD	ACTH, TNF-α, IL, IL-1β, serotonin (5-HT), dopamine (DA), and gamma-aminobutyric acid (GABA),SOD, CAT, MDA	Oral	GABAergic activity	Anxiolytic effects	Kim *et al.*, 2018

Silybumma-rianum	Milk thistle	Galactose, Xylose	EPM, OFT & FST	ACTH, TNF-α, IL, IL-1β, serotonin (5-HT), dopamine (DA),SOD, CAT, MDA	Oral	Antioxidant activity	Reduced stress-induced anxiety	Mazzanti *et al*., 2017
Camellia sinensis	Green tea	Glucose, Galactose	In vitro studies Cell culture	GABA, Serotonin, Dopamine, ROS, SOD, CAT and MTT Assay	Oral	Neurotra nsmitter modulation	Anxiety reduction observed	Unno *et al.*, 2019
Withania somnifera	Ashwa-gandha root	Glucose, Arabinose	EPM, OFT & FST	ACTH, TNF-α, IL, IL-1β, serotonin (5-HT), dopamine (DA),SOD, CAT, MDA	Oral	HPA axis modulation	Alleviation of anxiety symptoms	Chandra-sekhar *et al.*, 2012
Ziziphusjujuba	Jujube fruit	Glucose, Fructose	EPM, OFT & LD	ACTH, TNF-α, IL, IL-1β, serotonin (5-HT), dopamine (DA),SOD, TAC, GPx, MDA and H &E.	Oral	Neurotra nsmitter regulation	Reduced anxiety-like behavior	Zhang *et al*., 2021
Curcuma longa	Turmeric	Glucose, Rhamnose	EPM, OFT & LD	TNF-α, IL, IL-1β, serotonin (5-HT), dopamine (DA),SOD, CAT, MDA,TAC & H & E	Oral	Anti-inflamma tory effects	Reduced anxiety symptoms	Lau *et al*., 2020
Hibiscus sabdariffa	Hibiscus flower	Galactose, Glucose	EPM, OFT & LD	TNF-α, IL, IL-1β, serotonin (5-HT), dopamine (DA),SOD, CAT, MDA,GSH,TAC	Oral	Antioxidant effects	Anxiolytic properties observed	Hsieh *et al*., 2020
Salvia miltiorrhiza	Danshen root	Glucose, Fructose	EPM, OFT & LD	TNF-α, IL, IL-1β, serotonin (5-HT), dopamine (DA),SOD, CAT, MDA,GSH,TAC, BDNF, Caspas-3, Ach activity	Oral	Neuropro tection	Reduced anxiety-like behavior	Wang *et al.*, 2019
Schisandra chinensis	Schisa-ndra berries	Glucose, Galactose	EPM, OFT & LD	ACTH, CRH, serotonin (5-HT), dopamine (DA), GABA, SOD, CAT, MDA, GSH.	Oral	HPA axis modula-tion	Anxiolytic effects observed	Panossian *et al.*, 2013
Passiflora incarnata	Passion flower	Glucose, Fructose	EPM, OFT & Rotarod	GABA current, Modulation of GABA activty	Oral	GABAergic activity	Decreased anxiety symptoms	Cechinel Filho *et al.*, 2017

the hypothesis concerning the monoaminergic system. According to this hypothesis, anxiety is characterized by a reduction in levels of 5-hydroxytryptamine (serotonin), dopamine (DA), and nor epinephrine (NE) within the central nervous system. The pathogenesis of anxiety is rooted in the dysregulation of the 5-HT, DA, and NE neurotransmitter systems. The up regulation of type A monoamine oxidase (MAO-A) and the down regulation of serotonin (5-HT) and NE levels in the brain are considered primary etiological factors underlying anxiety. The MAO-A enzyme is responsible for the breakdown of monoamine neurotransmitters, including 5-HT, NE, and DA, and plays a significant role in the pathogenesis, progression, and treatment of various neuropsychiatric conditions[15]. Studies have shown that DA, 5-HT, and other neurotransmitters are crucial for maintaining chemical homeostasis within the brain. An imbalance, whether due to an excess or deficiency of these neurotransmitters, can lead to abnormalities in the brain's signaling system, ultimately resulting in the onset and development of anxiety disorders.

Angelica sinensis polysaccharide (ASP), one of the primary active compounds derived from *Angelica sinensi* has been found to significantly reduce the duration of forced swimming and immobility in mice with hanging tails at a dosage of 40 mg/kg[16] (Ding et al., 2021). Moreover, it enhances sugar-water preference, increases the levels of DA and 5-HT in the hippocampus, upregulates tryptophan hydroxylase mRNA expression, and elevates the GABA/Glu ratio-an essential rate-limiting enzyme involved in 5-HT synthesis, thereby regulating monoamine neurotransmitter transmission and rectifying excitatory-inhibitory imbalances in mice.

Polysaccharides act as antioxidant in anxiolytic activity :

Bioactive polysaccharides have emerged as potential protectors against oxidative stress, which is primarily driven by reactive oxygen species (ROS). These ROS are metabolic by-products that can contribute to neuronal degeneration by interfering with crucial biological molecules such as DNA, RNA, lipids, and proteins. Excessive ROS production due to oxidative stress can harm these biomolecules and cellular structures, ultimately leading to neuron death[9]. Recent research has demonstrated the neuroprotective properties of bioactive polysaccharides, showing their significant reducing power, antioxidant capacity, and ability to scavenge free radicals in vitro. Certain bioactive polysaccharides can lower ROS levels and reduce peroxidation products in both cellular and animal models experiencing oxidative stress. Additionally, these polysaccharides help mitigate oxidative damage by boosting the activity of various antioxidant enzymes, modulating gene expression, and influencing stress-related signaling pathways[18].

Polysaccharides Suppresses HPA axis :

Administration of *Polygonatum sibiricum* polysaccharide (PSP) significantly reduced CORT levels in mice subjected to LPS and chronic unpredictable mild stress (CUMS), indicating an inhibitory effect on HPA axis hyperactivity[21]. Additionally, *Lycium barbarum* polysaccharide (LBP) notably decreased the expression of the N-methyl-D-aspartate receptor 2B subunit (NR2B) and

calmodulin kinase II (CaMKII) proteins, lowered serum CORT levels, and improved the negative feedback regulation of the HPA axis, thereby alleviating anxiety-like behaviors in rats with post-traumatic stress disorder. In summary, polysaccharides can help alleviate anxiety-like behavior by reducing hyperactivity of the HPA axis. They effectively lower levels of CRH, ACTH, and CORT, promoting better negative feedback regulation of the HPA axis. Furthermore, polysaccharides may protect against hippocampal neuronal damage and dampen excessive activation of the HPA axis, leading to anxiolytic effects. This suggests a potential mechanism for polysaccharide-targeted interventions in anxiety disorders through modulation of the HPA axis.

Polysaccharides maintains neurotropic messengers :

The bioactive polysaccharide degraded porphyrin (DPR), extracted from *Porphyra haitanensis*, and was used by Yi *et al*. to mitigate anxiety-like behaviors in LPS-treated mice. This treatment activated the BDNF/TrkB/ERK/CREB signaling pathway in the hippocampus of CUMS mice, presenting a potential therapeutic strategy for anxiety[25,26] found that alcohol-soluble polysaccharides from *Dendrobium officinale* flowers offer additional protection against neuronal apoptosis and help maintain the 5-HT system by activating the BDNF/TrkB/CREB pathway (Liu et. al.) examined the combined effects of Lily polysaccharide (LLP) and Astragalus polysaccharide (APS) in a specific ratio on anxiety-like behaviors and their modulation of the adenylyl cyclase/cyclic adenosine monophosphate/protein kinase A (AC/cAMP/PKA) signaling pathway in mice subjected to chronic stress[16].

Polysaccharides regulates inflammatory mediators :

Polygonatum sibiricum polysaccharide (PSP) may exhibit anxiolytic effects by inhibiting the activation of NF-κB expression and its nuclear translocation in mouse models of anxiety induced by LPS and chronic unpredictable stress (CUS)[20]. Additionally, PSP reduces the levels of pro-inflammatory factors IL-1β and TNF-α in hippocampal tissues. Endogenous ligands released during brain injury activate Toll-like receptor 4 (TLR4), which subsequently triggers NF-κB activation through the MyD88-dependent signaling pathway, leading to the transcription of various pro-inflammatory factors[5]. PSP has shown inhibitory effects on the upregulation of NLRP3, ASC, caspase-1, cleaved-caspase-1, and IL-1β in an LPS-induced anxiety model in mice.

Polysaccharides alter the Tryptophan metabolism :

Intervention with *Polygonatum sibiricum* polysaccharides (PSP) was shown to downregulate TRP and 3-HK levels in the hippocampus of mice in a behavioral despair model[24]. Additionally, the observed increase in 5-HT levels suggests that these polysaccharides may influence TRP metabolism by enhancing TPH enzyme activity while inhibiting IDO enzyme activity, thereby favoring the TRP/5-HT pathway[26]. PSP may reduce kynurenine metabolism and lower downstream 3-HK levels, contributing to their anxiolytic effects. The total glycosides (TG) of *Cistanche*

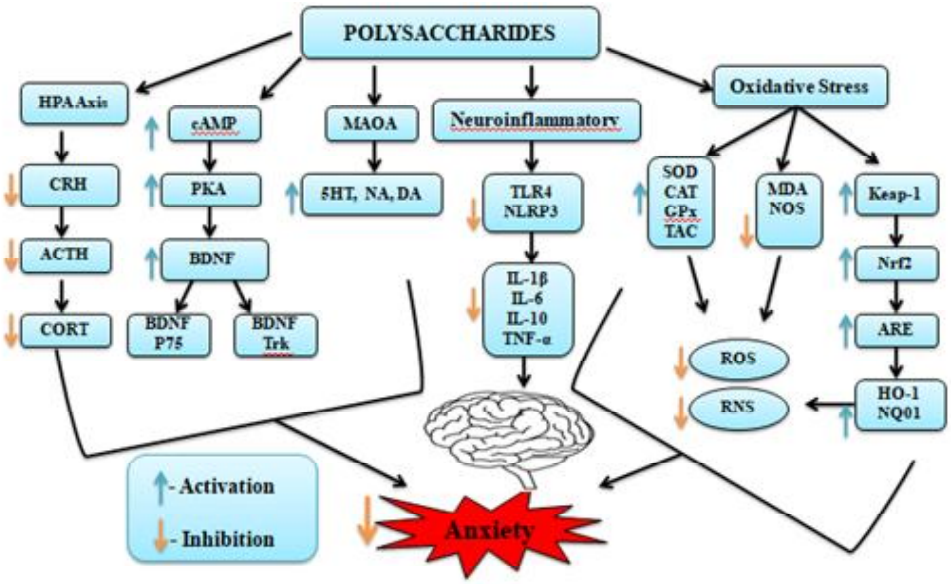

Fig. 2. Mechanism of Action of Polysaccharides

tubulosa significantly increased serum TRP levels in chronically unpredictable stressed rats ($p < 0.05$) while decreasing serum KYN levels and the KYN/TRP ratio ($p < 0.05$) (Fan et al., 2021). Concurrently, they downregulated the expression of IDO protein in both the colon and hippocampus of rats ($p < 0.05$). These results indicate that these glycosides inhibit TRP metabolism into kynurenine, thereby promoting the conversion of TRP to serotonin and exerting an anxiolytic effect.

HPA: Hypothalamus Pituitary Adrenal **BDNF:** Brain-derived neurotrophic factor **NLRP**: Nucleotide domain, Leucine rich Pyrin **MDA:** Malondialdehyde **CRH**: Corticotropin releasing hormone **MAOA:** Monoamine oxidase A **IL-1β:** Interleukin 1β **NOS**: Nitric Oxide **5 -HT:** 5- Hydroxytryptamine **Nrf2:** Nuclear factor erythroid 2–related factor 2	**IL-6 :** Interleukin 6 **ROS:** Re active Oxygen Species **CORT**: Cortisole **NA:** Noradrenaline **IL-10:** Interleukin 10 **RNS:** Re active Nitrogen Species **cAMP:** Cyclic Adenosine-monophosphate **ACTH:** Adreno corticotropic hormone **Keap1:** Kelch-like ECH-associated protein 1 **HO1:** Heme oxygenase	**TLR:** Toll like receptor **SOD:** Superoxide dismutase **CAT:** Catalase **GPx:** Gulathione Peroxidase **TAC:** Total Antioxidant Capacity **DA:** Dopamine **TNF-α:** Tumour Necrosis Factor α **PKA:** Protein Kinase A **NQ01:** Quinone oxidoreductase **ARE:** Antioxidant Response Element

Conclusion and Prospects :

Due to the complex nature of anxiety, current anxiolytic medications often have limited effectiveness and can be associated with significant side effects. This creates a pressing need for the development of drugs that can effectively prevent or treat anxiety while minimizing adverse reactions. Natural plants, derived from various sources, generally pose minimal harm to the human body and have the advantage of targeting multiple pathways simultaneously. Several traditional Chinese medicine polysaccharide products, such as Astragalus polysaccharide injections, Ginseng polysaccharide injections, and *Poriacocos* acidic polysaccharide oral solutions, have been introduced for clinical use due to their immunomodulatory effects, particularly in enhancing the immune system in patients undergoing chemotherapy.

Research has shown that natural plant polysaccharides can exert anxiolytic effects through various mechanisms, including the regulation of neurotransmitters and their receptors, modulation of the HPA axis, control of inflammatory responses, management of oxidative stress, modulation of neurotrophic factors, and regulation of gut microbiota and tryptophan metabolism. In experimental studies of natural plant polysaccharide anxiolytics, researchers have utilized various stress models, such as chronic unpredictable mild stress, social isolation stress, social defeat stress, post-traumatic stress disorder, and acute behavioral despair. It is also important to recognize that individuals with anxiety often experience comorbid psychiatric disorders, such as obsessive-compulsive disorder and depression. Future studies should therefore evaluate the effectiveness of polysaccharides in models that incorporate these comorbidities and explore combination therapies to enhance anxiety treatment.

Many studies have confirmed the anxiolytic effects of natural plant polysaccharides and shed light on their mechanisms of action from various perspectives. Ongoing research continues to reveal additional insights into how these polysaccharides may alleviate anxiety. As a primary bioactive component of plants, natural plant polysaccharides exhibit a wide range of biological activities. Thus, investigating their anxiolytic effects is crucial for the development and application of natural plant-based polysaccharide products.

In conclusion, natural polysaccharides derived from plant sources offer valuable potential for investigating the mechanisms underlying anxiety and may serve as a foundation for future research on these compounds. Their development as anxiolytics with minimal side effects and high efficacy could significantly expand treatment options for anxiety disorders.

References :

1. Adolphs, R., D. Tranel and A.R. Damasio, (1998). *Nature, 393*(6684): 470-474. https://doi.org/10.1038/30982
2. American Psychiatric Association. (2013). Diagnostic and statistical manual of mental disorders (5th ed.). American Psychiatric Association.
3. Bandelow, B., J. Zohar, E. Hollander, S. Kasper, and H. J. Möller, (2002). *World Journal of Biological Psychiatry, 3*(4): 171-199. https://doi.org/10.3109/15622970209150607
4. Baxter, A. J., K. M. Scott, A. J. Ferrari, and H.A. Whiteford, (2013). *Psycholo-*

gical Medicine, 43(5): 897-910. https://doi.org/10.1017/S003329171200147X
5. Brancato, S. K., and J. E. Albina, (2013). *Journal of Immunology, 190*(1): 3-12.
6. Davis, M. (2006). Fear and anxiety: *American Psychologist, 61*(3): 255-265. https://doi.org/10.1037/0003-066X.61.3.255
7. Ding, X., L. Wang, Y. Zhang, and Z. Zhang, (2021). *Phytomedicine, 80:* 153378. https://doi.org/10.1016/j.phymed.2020.153378
8. Fan, J., J. Zhang, M. Liu, Y. Wang, and J. Li, (2021). *Phytomedicine, 81:* 153402. https://doi.org/10.1016/j.phymed.2020.153402
9. Gao, X., L. Wang, Y. Li, and J. Zhang, (2018). *Journal of Neurochemistry, 147*(1): 3-18. https://doi.org/10.1111/jnc.14521
10. Greenberg, D. B., R. E. Wiegand, and M. Goldstein, (2007). *Biological Psychiatry, 61*(1): 3-12. https://doi.org/10.1016/j.biopsych.2006.05.010
11. Grinchii, V., and E. Dremencov, (2020). *Journal of Psychopharmacology, 34*(8): 931–944. https://doi.org/10.1177/0269881120908486
12. Ji, X., Y. Liu, H. Xu, and Q. Zhao, (2023). *Frontiers in Pharmacology, 14:* 669798. https://doi.org/10.3389/fphar.2023.669798
13. Kessler, R. C., P. Berglund, O. Demler, R. Jin, K.R. Merikangas and E.E. Walters, (2005). *Archives of General Psychiatry, 62*(6): 593-602. https://doi.org/10.1001/archpsyc.62.6.593
14. LeDoux, J. E. (2000). *Annual Review of Neuroscience, 23:* 155-184. https://doi.org/10.1146/annurev.neuro.23.1.155
15. Liu, F., Y. Li and X. Zhang (2019). *Frontiers in Pharmacology, 10:* 883. https://doi.org/10.3389/fphar.2019.00883
16. Liu, P., M. Zhang, and H. Li, (2022). *Journal of Experimental Biology, 70*(5): 1023-1032.
17. Mu, L., H. Li, Y. Wang, and Z. Zhang, (2021). *Journal of Natural Products, 84*(2): 451–468. https://doi.org/10.1021/acs.jnatprod.0c01090
18. Radley, J. J., and P. E. Sawchenko, (2011). *In Advances in Experimental Medicine and Biology, 716:* 127-149. Springer. https://doi.org/10.1007/978-1-4419-1673-7_8
19. Roy-Byrne, P. P., M. B. Stein, and D. H. Barlow, (2008). *Psychiatric Clinics of North America, 31*(4): 625-644. https://doi.org/10.1016/j.psc.2008.06.003
20. Shen, X., W. Liu, and Y. Wang, (2021). *Journal of Neuroinflammation, 18*(1): 33-45.
21. Shen, Y., J. Zhang, and Y. Li, (2021). *Phytomedicine, 79:* 153345. https://doi.org/10.1016/j.phymed.2020.153345
22. Ulrich-Lai, Y.M. and J.P. Herman, (2009). *Nature Reviews Neuroscience, 10*(6): 397 409. https://doi.org/10.1038/nrn2647
23. Wang, S., X. Li, M. Zhang, and J. Liu, (2020). *Neurochemistry International, 140:* 104792. https://doi.org/10.1016/j.neuint.2020.104792
24. Wei, Z., S. Zhang, Z. Wang, L. Zhang and Y. Zhang, (2022). *Journal of Ethnopharmacology, 290:* 115065. https://doi.org/10.1016/j.jep.2022.115065
25. Yang, L., J. Wang, and Y. Li, (2022). *Neuropharmacology, 134:* 54-66.
26. Yi, Y., S. Zhang and X. Li (2021). *Journal of Neuroscience Research, 49*(3): 123-136.
27. Zhang, Y., W. Liu, and P. Chen, (2021). Mechanisms of oxidative stress mitigation by polysaccharides: Enzyme modulation and gene expression. *Antioxidants, 10*(8): 1234. https://doi.org/10.3390/antiox10081234