Research Article

Protective and Therapeutic Role of Ajwa Date Extract in Propionic Acid–Induced Autism in Rats

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Abstract | Environmental chemical exposure is increasingly implicated in developmental neurotoxicity and autism spectrum disorder (ASD). Animal models provide valuable insights into neurotoxic triggers and potential protective interventions. This study evaluated the preventive and therapeutic potential of Ajwa date aqueous extract (JDE) against propionic acid (PPA)-induced neurotoxicity in rats, focusing on oxidative stress, inflammation and serotonergic dysregulation. Thirty-two male rats were randomised into four groups (n = 8 each). Group A (control) received no treatment, group B received oral PPA (250 mg/kg/day, 3 days), group C (therapeutic) received PPA (250 mg/kg/day, 3 days) followed by JDE (1.0 g/kg/day, 14 days) and group D (preventive) received PPA (100 mg/kg/day, 14 days) and JDE (0.5 g/kg/day, 14 days). The biomarkers assessed included the levels of antioxidant enzymes superoxide dismutase (SOD) and malondialdehyde (MDA), pro-inflammatory cytokine tumour necrosis factor α (TNF-α) and serotonin. PPA exposure markedly elevated MDA (10.12 ± 2.13 vs. control 5.97 ± 0.51; $p < 0.001$), TNF-α (325.7 ± 0.38 vs. control 199.5 ± 3.3; $p < 0.001$) and serotonin (143.5 ± 0.03 vs. control 122.67 ± 0.08; $p < 0.001$)), while significantly reducing SOD activity (3.22 ± 0.43 vs. control 7.89 ± 0.32; $p < 0.001$). Therapeutic JDE (group C) improved SOD (5.57 ± 2.34 vs. PPA 3.22 ± 0.43; $p < 0.001$) and reduced TNF-α (233.2 ± 0.42 vs. PPA 325.7 ± 0.38; $p < 0.001$), though MDA remained elevated (4.75 ± 1.86 vs. control 5.97 ± 0.51; $p < 0.05$). Preventive JDE (group D) showed the most pronounced antioxidant protection, SOD level was restored nearly to control levels and TNF-α level significantly reduced (4.33 ± 0.19 and 262.8 ± 0.38 vs. PPA 3.22 ± 0.43 and 325.7 ± 0.38; $p < 0.01$). Serotonin levels were partially normalised in both JDE groups. JDE demonstrated partial preventive and therapeutic effects against PPA-induced neurotoxicity primarily by modulating oxidative stress, inflammation and serotonergic imbalance. These findings highlight JDE as a potential preclinical neuroprotective agent, warranting further molecular and translational studies.

Keywords | Ajwa date extract, Propionic acid, Autism spectrum disorder, Oxidative stress, Gut–brain axis

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INTRODUCTION

Autism encompasses a range of characteristics likely stemming from a cluster of neurodevelopmental brain conditions with a considerable genetic foundation. These conditions are marked by developmental challenges in language and social interaction abilities, the emergence of repetitive or irregular movements (Chauhan and Chauhan, 2006), hyperactivity, sensory issues, limited interests and occasional self-harm. The causes and mechanisms remain elusive, although various factors, such as immune responses, environmental influences, neurochemical imbalances, genetic predispositions and oxidative stress, have been found to contribute to autism (Jenner, 2003). Oxidative stress is a key factor in the development of neurological disorders, including autism, schizophrenia, Parkinson's disease, Down

syndrome and Alzheimer's disease, according to a number of studies (Bowers *et al*., 2011). Along with other short-chain fatty acids (SCFAs) produced by gut bacteria, such as acetate and butyrate, propionic acid (PPA), which is a byproduct in fatty acid metabolism, is present at high concentrations in the gut. By entering the brain and exerting negative effects on the central nervous system, PPA may influence behavioural, neuropathological and biochemical abnormalities associated with autism (Grafodatskaya *et al*., 2010). Recent studies after 2020 have highlighted consistent alterations in gut microbiota composition in individuals with autism spectrum disorder (ASD), demonstrating increased abundance of SCFA producers, such as propionate, and reduced levels of butyrate-producing species (Lagod and Naser, 2023). These microbial changes are implicated in gut–brain axis dysfunction through mechanisms involving neurotransmitter modulation, immune activation and oxidative stress. Although dietary preferences in ASD populations may partially account for these microbial differences, experimental evidence supports a causal contribution of SCFAs, particularly PPA, in inducing autism-like behaviours and oxidative imbalance in animal models. Dietary polyphenols and flavonoids can reshape gut microbial ecology, enhance antioxidant defences (e.g. glutathione [GSH] pathways) and attenuate neuroinflammatory signalling, showing potential applications in protective or therapeutic interventions against PPA-induced neurotoxicity. However, well-controlled clinical trials are still required to confirm their efficacy and safety in ASD management (Liu *et al*., 2019).

Date fruit provides antioxidant phenolic chemicals and has nutritional benefits. The antioxidant properties of Algerian dates (Khan *et al*., 2017; Greenman *et al*., 2024; Ukkirapandian *et al*., 2024) have been explored, and phenolic acid concentration varies between fresh and dried dates. Ajwa dates possess hypolipidemic, antioxidant, anti-inflammatory, cardioprotective, nephroprotective and hepatoprotective properties (Tchaconas and Adesman, 2013). Simple phenolics, such as p-hydroxybenzoic acid, protocatechuic acid, gallic acid, vanillic acid and syringic acid, are among the many pharmacologically relevant phytochemicals found in date fruit (Shultz *et al*., 2008). Traditionally, date palm has been used to treat psychosis, anxiety, cognitive deficits and various nervous system disorders (Patterson and Holahan, 2012; Saeed *et al*., 2025). This study investigates the potential protective and preventive effects of oral Ajwa date supplementation in alleviating persistent biochemical autistic traits in PPA-treated rats.

MATERIALS AND METHODS

Animals

The 32 male Western albino rats used in this experiment were obtained from the animal facility at Thi-Qar University's College of Sciences. They were approximately 21 days old and weighed between 45 and 60 g. The following conditions were used: 12 h light/12 h dark cycle, constant temperature, unrestricted access to tap water and regular laboratory feed. The rats were acclimated for seven days before being randomly assigned to four groups of eight. The control group (group A) received no treatment. For three days, group B received oral PPA at a dose of 250 mg/kg body weight per day to induce traits resembling autism. In group C (treatment group), 1.0 g/kg body weight of Ajwa date aqueous extract (JDE) orally was administered for two weeks after three days of 250 mg/kg body weight per day of PPA. Group D (preventative group) received 100 mg/kg body weight of PPA and 0.5 g/kg body weight of JDE every day for two weeks.

Preparation of Ajwa date aqueous extract (JDE)

Ajwa dates were purchased from local markets in Thi-Qar, Iraq. The flesh of the dates was separated and extracted using ultrapure distilled water in a ratio of 1:3 (w/v) under continuous stirring. The mixture was incubated at 25 °C for 48 h on a rotary shaker set at 60 rpm. The suspension was first filtered through muslin cloth and then through Whatman No. 1 filter paper. The obtained filtrate was centrifuged at 4500 rpm for 10 min, and the resulting supernatant was re-filtered. The final aqueous extract was aliquoted and stored at −80 °C until further use.

Collection of blood samples

Blood was collected via cardiac puncture with a disposable syringe and placed in plain tubes. The samples were spun at 3000 rpm for 10 min, and the separated serum was transferred to several Eppendorf tubes. The serum was either analysed immediately or stored at 4 °C for subsequent biochemical testing.

Measurement of serum malondialdehyde

Serum levels of malondialdehyde (MDA), which is an important indicator of lipid peroxidation, was determined using the method described earlier (Hasan *et al*., 2025). An assay kit for thiobarbituric acid reactive compounds was used. The reaction mixture contained 1 mL of serum, sodium dodecyl sulphate, 1.5 mL of 0.37% thiobarbituric acid (TBA) diluted in 50 mM NaOH and 1 mL of 2.8% acetic acid. Incubation in a water bath for 20 min resulted in the formation of an MDA-TBA chromogenic complex. Following 2 min of centrifugation at 1500 rpm, the supernatant was collected and a spectrophotometer was used to measure the absorbance of the resultant pink complex at 532 nm. The data were calibrated against a standard curve. The unit of measurement for MDA concentrations was nmol/mg.

Superoxide dismutase (SOD) assay

Nitro blue tetrazolium (0.6 mL), sodium pyrophosphate (1.2 mL), phenazine methosulphate (0.1 mL) and distilled water (2.8 mL) were mixed. The resulting reaction solution was measured in terms of superoxide dismutase (SOD) activity. The procedure began with the addition of 0.2 mL of nicotinamide adenine dinucleotide hydrogen. Glacial acetic acid (1 mL) was added to the mixture to halt the process after 2 min of incubation at 30 °C. After the addition of 4 mL of n-butanol, the mixture was thoroughly mixed and allowed to stand for 10 min. A spectrophotometer was used to measure the coloured complex's absorbance at 560 nm.

Tumour necrosis factor (TNF) α assay

Following the manufacturer's instructions, we measured TNF-α levels with a sandwich enzyme-linked immunosorbent assay (ELISA). Each duplicate was mixed with 100 µL of the standard solution, covered and incubated at 37 °C for 90 min. Then, 100 µL of biotinylated detection antibody was quickly added to each well after the liquid was removed. The wells were then incubated at 37 °C for an hour. Each wash required 350 µL of wash buffer and performed for 1–2 min. The plate was incubated at 37 °C for 30 min following the addition of the horseradish peroxidase conjugate solution. After five washes, the plate was incubated with the substrate reagent for 15 min at 37 °C. A microplate reader was used to quantify the optical density at 450 nm after the reaction's cessation with 50 µL of stop solution (Hasan *et al*., 2025).

Serotonin assay

We used a competitive ELISA method to quantify serotonin concentrations in accordance with the manufacturer's instructions. Quantitative acylation of serotonin was performed. After the addition of 25 µL of acylated standards, the controls and samples were added to the appropriate wells, and then 100 µL of serotonin antiserum was added to each well of the serotonin microtiter strips. After 30 min, the plate was sealed and incubated for another hour at room temperature. The wells were washed with 300 µL of wash buffer, and then 100 µL of conjugate was added. The wells were then shaken at 600 rpm for 15 min at room temperature. The substrate (100 µL) was added after another 15 min of incubation, and the washing process was repeated. The plate was shaken for 15 min at room temperature before the 0.25 M H_2SO_4 stop solution was added. The absorbance of the coloured product was 450 nm (Hasan *et al*., 2024).

Statistical analysis

To analyse serum data, we employed one-way analysis of variance (ANOVA Tukey). We computed the control and treatment groups' mean values, standard deviations (mean ± SD) and differences. A p-value of less than 0.05 was considered statistically significant (Karakose *et al*., 2016).

RESULTS

In group B, rats administered with PPA exhibited markedly increased MDA and TNF-α levels (10.12 ± 2.13 and 325.7 ± 0.38). Tables 1 and 2 reflect heightened oxidative stress and inflammatory responses. SOD activity was reduced (3.22 ± 0.43; Table 1), and serotonin levels were elevated (143.5 ± 0.03; Table 2). By contrast, group C, which received therapeutic JDE treatment, showed enhanced SOD levels (5.57 ± 2.34; Table 1) and reduced TNF-α level (233.2 ± 0.42; Table 2), although MDA levels remained higher than those in the control group. Group D, which was subjected to preventive JDE treatment, displayed the most significant decrease in TNF-α level (262.8 ± 0.38; Table 2) and improved antioxidant capacity with elevated SOD levels (4.33 ± 0.19; Table 1), but MDA levels were still high. Both JDE-treated groups demonstrated a modest normalisation of serotonin levels, compared with the PPA-only group (Tables 1 and 2).

Table 1: Serum malondialdehyde (MDA) and superoxide dismutase (SOD) levels in control and JDE-treated rats.

Parameters/ Groups	MDA (nm/mg)	SOD (mmol/mg)
A (Control)	5.97 ± 0.51^{b}	7.89 ± 0.32^{a}
B (PPA treatment (250 mg/kg))	10.12 ± 2.13^{c}	3.22 ± 0.43^{c}
C (JDE (1.0 g/kg bw) + PPA (250 mg/kg bw))	4.75 ± 1.86^{a}	5.57 ± 2.34^{b}
D (JDE (0.5 g/kg bw) + PPA (100 mg/kg bw))	3.96 ± 1.05^{a}	4.33 ± 0.19^{b}

Data are expressed as mean ± SD (n = 8). The different superscript letters refer to significant difference ($p \leq 0.05$). PPA: Propionic Acid, JDE; Ajwa Date Aqueous Extract.

Table 2: Tumor Necrosis Factor (TNF)-α and serotonin levels in control and JDE-treated rats

Parameters/ Groups	TNF-α (pg/mg)	Serotonin (ng/ml)
A (Control)	199.5 ± 3.3^{c}	122.67 ± 0.08^{c}
B (PPA treatment (250 mg/kg))	325.7 ± 0.38^{a}	143.5 ± 0.03^{a}
C (JDE (1.0 g/kg bw) + PPA (250 mg/kg bw))	233.2 ± 0.42^{b}	128.6 ± 0.26^{b}
D (JDE (0.5 g/kg bw) + PPA (100 mg/kg bw))	262.8 ± 0.38^{b}	131.4 ± 0.05^{b}

Data expressed as mean ± SD (n = 8). The different superscript letters refer to significant difference ($p \leq 0.05$); PPA: propionic acid; JDE: Ajwa Date Extract.

DISCUSSION

Ajwa date extract (JDE) exerts therapeutic and protective effects against neurotoxic damage, and the

current study offers strong evidence that oxidative stress and neuroinflammation are important factors in the development of autism-like traits caused by PPA.

Oxidative stress and antioxidant defence

MDA levels considerably increased and SOD activity decreased in the PPA-treated group, suggesting increased lipid peroxidation and weakened antioxidant defences. These findings align with previous research highlighting elevated oxidative stress in autism models (Metwally *et al*., 2024) and in neurodegenerative conditions, such as Alzheimer's and Parkinson's (de Matos Feijó *et al*., 2013). Bowers *et al*. (2011) identified genetic disruptions in the GSH system in ASD patients, pointing to a predisposition to oxidative imbalance (Finamor *et al*., 2017). Additionally, valproic acid, akin to PPA, alters antioxidant gene expression through epigenetic mechanisms, exacerbating oxidative damage (Finamor *et al*., 2021). Treatment with JDE markedly improved SOD levels and decreased MDA, suggesting enhanced antioxidant capacity. This effect is likely due to the presence of proanthocyanidins and polyphenolic compounds in Ajwa dates, which are known to boost GSH, CAT and GPx enzyme activities. The phytochemicals present in Ajwa dates include polyphenols, flavonoids and phenolic acids, which exert pleiotropic effects on molecular pathways implicated in ASD (El-Ansary and Al-Ayadhi, 2012). These bioactive compounds modulate oxidative stress by enhancing endogenous antioxidant defences, such as GSH synthesis and the activity of GSH peroxidase, thereby counteracting the excessive production of reactive oxygen species (ROS) induced by PPA and other gut-derived metabolites. Polyphenols act as potent regulators of neuroinflammation by inhibiting pro-inflammatory mediators (e.g. TNF-α, IL-6 and NF-κB signalling and restoring microglial homeostasis, which are often disrupted in ASD (Kundu and Surh, 2008).

Notably, the gut–brain axis provides an integrative framework for understanding how Ajwa date phytochemicals may influence neurodevelopmental outcomes. Polyphenols and flavonoids serve as prebiotic-like substrates that shape gut microbial composition, enhancing the abundance of beneficial bacteria and suppressing potentially pathogenic taxa (Strandwitz, 2018). This microbial remodelling not only alters the profile of SCFAs but also may attenuate the overproduction of propionate, which is a metabolite strongly linked to ASD-like phenotypes. Additionally, the biotransformation of polyphenols by gut microbes yields bioactive metabolites with systemic neuroprotective effects, including the modulation of neurotransmitter systems, such as serotonin, dopamine and In summary, Ajwa date phytochemicals may act through a dual mechanism: direct antioxidant and anti-inflammatory modulation of molecular pathways involved in oxidative stress, apoptosis and synaptic plasticity and indirect regulation of the gut–brain axis through the restoration of microbial balance and reduction of neurotoxic SCFA burden (Hranilovic *et al*., 2007). This integrative action highlights the therapeutic promise of JDE as a natural neuroprotective intervention in the PPA-induced models of ASD, underscoring the centrality of the gut–brain axis as a mechanistic target in contemporary autism research (Finamor *et al*., 2014). Numerous studies have found a link between increased oxidative stress and the emergence of neurodegenerative diseases, including Parkinson's, Alzheimer's and ASD (Martinez-Micaelo *et al*., 2012). The autism-induced group in this investigation displayed decreased SOD and increased MDA, which are signs of lipid peroxidation, in line with previous studies (Hammock *et al*., 2012). Valproate's epigenetic effects may have increased oxidative stress in the autism group. However, Bowers *et al*. (2011) found genetic differences in the glutathione-like antioxidant system in children with ASD.

Neuroinflammation and cytokine profile

Exposure to PPA led to a considerable increase in TNF-α, which is a pro-inflammatory cytokine, in the hippocampal region, confirming an enhanced neuroinflammatory response. This finding is consistent with prior studies (Asdaq *et al*., 2024). The activation of NF-κB, which is a key regulator of inflammation, has been observed in ASD patients (Fossati and Prencipe, 1982). JDE treatment markedly reduced TNF-α levels, demonstrating anti-inflammatory properties. This finding is in line with earlier findings that proanthocyanidins can suppress TNF-α expression while promoting anti-inflammatory cytokines, such as IL-12, which facilitate the regulation of immune responses and alleviation of tumour-promoting inflammation (Gulec *et al*., 2006).

Serotonin dysregulation

The autism-induced group displayed a notable elevation in brain serotonin levels, consistent with hyperserotonaemia commonly observed in children with ASD (Kılıç *et al*., 2025). Serotonin is critical for brain development, and its dysregulation is associated with impaired synaptic signalling and behavioural abnormalities (Al-Gadani *et al*., 2009; Alkufi and Kassab, 2024). JDE treatment partially normalised serotonin levels potentially by mitigating oxidative and inflammatory stress, which are known to affect serotonin metabolism (Vaughan, 2011; Alkufi and Kassab, 2025).

CONCLUSION

JDE demonstrated prophylactic and therapeutic efficacy in attenuating PPA-induced neurotoxicity in rats. The

administration of JDE partially restored antioxidant defence mechanisms, suppressed neuroinflammatory signalling and ameliorated disruptions in neurotransmitter pathways. Collectively, these findings support the potential neuroprotective capacity of JDE but are preliminary and preclinical in nature. Thus, mechanistic elucidation and rigorous validation in clinical studies are needed.

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NOVELTY STATEMENT

Our study provides strong evidence that Ajwa Date Extract positively influences the Autism in Rats. These findings offer new insights into preventive and therapeutic potential of Ajwa date aqueous extract (JDE) against propionic acid (PPA)-induced neurotoxicity in rats, focusing on oxidative stress, inflammation and serotonergic dysregulation. Due to their potent antioxidant and anti-inflammation properties, these compounds could be further explored and extracted for use in the pharmaceutical and nutraceutical industries.

AUTHOR'S CONTRIBUTION

HKA: Data collection, investigation, methodology, writing original draft preparation. ATK: Project administration. SAH: Writing review. NASN: Approve the final version of the manuscript.

Ethical standard

The research received approval from the ethics review board at the University of Thi-Qar's College of Pharmacy (Approval No. IRB01092023, dated 01/09/2023). All procedures adhered to the guidelines set by the animal ethics committee. In vivo experiments were conducted using an appropriate number of healthy Sprague–Dawley rats.

Data availability

Data will be made available on request.

Generative AI and AI-assisted technology statement

The authors declare that no Genrative AI was used in the creation of this manuscript.

Conflict of interest

The authors have declared no conflict of interest.

REFERENCES

Al-Gadani Y, El-Ansary A, Attas O, Al-Ayadhi L (2009). Metabolic biomarkers related to oxidative stress and antioxidant status in Saudi autistic children. Clin. Biochem., 42: 1032–1040. https://doi.org/10.1016/j.clinbiochem.2009.03.011

Alkufi HK, Kassab HJ (2024). Soluplus-stabilized nimodipine-entrapped spanlastic formulations prepared with edge activator (Tween20): Comparative physicochemical evaluation. Pharm. Nanotechnol., 13: 551-563. https://doi.org/10.2174/0122117385348551241028102256

Alkufi HK, Kassab HJ (2025). Nanospanlastic in situ gel for nose to brain delivery of nimodipine: *In vitro* optimization and *in vivo* pharmacokinetic study. Al-Rafidain J. Med. Sci., 8: 97–105. https://doi.org/10.54133/ajms.v8i1.1687

Asdaq SMB, Almutiri AA, Alenzi A, Shaikh M, Shaik MA, Alshehri S, Rabbani SI (2024). Unveiling the neuroprotective potential of date palm (*Phoenix dactylifera*): A systematic review. Pharmaceuticals (Basel), 17: 1221. https://doi.org/10.3390/ph17091221

Bowers K, Li Q, Bressler J, Avramopoulos D, Newschaffer C, Fallin MD (2011). Glutathione pathway gene variation and risk of autism spectrum disorders. J. Neurodev. Disord., 3: 132–143. https://doi.org/10.1007/s11689-011-9077-4

Chauhan A, Chauhan V (2006). Oxidative stress in autism. Pathophysiology, 13: 171–181. https://doi.org/10.1016/j.pathophys.2006.05.007

de Matos Feijó F, Ballard CR, Foletto KC, Batista BAM, Neves AM, Ribeiro MFM, Bertoluci MC (2013). Saccharin and aspartame, compared with sucrose, induce greater weight gain in adult Wistar rats, at similar total caloric intake levels. Appetite, 60: 203–207. https://doi.org/10.1016/j.appet.2012.10.009

El-Ansary A, Al-Ayadhi L (2012). Neuroinflammation in autism spectrum disorders. J. Neuroinflamm., 9: 265. https://doi.org/10.1186/1742-2094-9-265

Finamor I, Pérez S, Bressan CA, Brenner CE, Rius-Pérez S, Brittes PC, Sastre J (2017). Chronic aspartame intake causes changes in the trans-sulphuration pathway, glutathione depletion and liver damage in mice. Redox Biol., 11: 701–707. https://doi.org/10.1016/j.redox.2017.01.019

Finamor IA, Bressan CA, Torres-Cuevas I, Rius-Pérez S, da Veiga M, Rocha MI, Pérez S (2021). Long-term aspartame administration leads to fibrosis, inflammasome activation, and gluconeogenesis impairment in the liver of mice. Biology (Basel)., 10: 82. https://doi.org/10.3390/biology10020082

Finamor IA, Ourique GM, Pês TS, Saccol EMH, Bressan CA, Scheid T, Pavanato MA (2014). The protective effect of N-acetylcysteine on oxidative stress in the brain caused by the long-term intake of aspartame by rats. Neurochem. Res., 39: 1681–1690. https://doi.org/10.1007/s11064-014-1360-9

Fossati P, Prencipe L (1982). Serum triglycerides determined colorimetrically with an enzyme that produces hydrogen peroxide. Clin. Chem., 28: 2077–2080. https://doi.org/10.1093/clinchem/28.10.2077

Grafodatskaya D, Chung B, Szatmari P, Weksberg R (2010). Autism spectrum disorders and epigenetics. J. Am. Acad. Child Adolesc. Psych., 49: 794–809. https://doi.org/10.1016/j.jaac.2010.05.005

Greenman N, Abdelli LS, Hassouneh SAD, Ali S, Johnston C, Naser SA, Azarian T (2024). Impact of propionic acid-

rich diets on microbial composition of the murine gut microbiome. Front Microbiomes., 3: 1451735. https://doi.org/10.3389/frmbi.2024.1451735

Gulec M, Gurel A, Armutcu F (2006). Vitamin E protects against oxidative damage caused by formaldehyde in the liver and plasma of rats. Mol. Cell Biochem., 290: 61–67. https://doi.org/10.1007/s11010-006-9165-z

Hammock E, Veenstra-VanderWeele J, Yan Z, Kerr TM, Morris M, Anderson GM, Jacob S (2012). Examining autism spectrum disorders by biomarkers: example from the oxytocin and serotonin systems. J. Am. Acad. Child Adolesc. Psych., 51: 712–721. https://doi.org/10.1016/j.jaac.2012.04.010

Hasan SA, Abass AA, Jabbar L (2025). The protective role of ethanolic extract of ginseng (*Panax ginseng*) against adverse physiological and histological alterations in the liver of female rabbits exposed to chlorine. Adv Life Sci., 12: 185–190. https://doi.org/10.62940/als.v12i1.2537

Hasan SA, Al-Rikaby AA, Al-Rikaby MA (2024). Evaluation of oxidative stress and some biochemical criteria in male rabbits following administration of aspartame. J. Anim. Hlth. Prod., 12: 75–80. https://doi.org/10.17582/journal.jahp/2024/12.s1.75.80

Hranilovic D, Bujas-Petkovic Z, Vragovic R, Vuk T, Hock K, Jernej B (2007). Hyperserotonemia in adults with autistic disorder. J. Autism. Dev. Disord., 37: 1934–1940. https://doi.org/10.1007/s10803-006-0324-6

Jenner P (2003). Oxidative stress in Parkinson's disease. Ann. Neurol. Off. J. Am. Neurol. Assoc. Child. Neurol. Soc., 53: S26–S38. https://doi.org/10.1002/ana.10483

Karakose M, Demircan K, Tutal E, Demirci T, Arslan MS, Sahin M, Cakal E (2016). Clinical significance of ADAMTS1, ADAMTS5, ADAMTS9 aggrecanases and IL-17A, IL-23, IL-33 cytokines in polycystic ovary syndrome. J Endocrinol Invest., 39: 1269–1275. https://doi.org/10.1007/s40618-016-0472-2

Khan F, Khan TJ, Kalamegam G, Pushparaj PN, Chaudhary A, Abuzenadah A, Al-Qahtani M (2017). Anti-cancer effects of Ajwa dates (Phoenix dactylifera L.) in diethylnitrosamine induced hepatocellular carcinoma in Wistar rats. BMC Complement. Altern. Med., 17: 418. https://doi.org/10.1186/s12906-017-1926-6

Kılıç KD, Garipoğlu G, Çakar B, Uyanıkgil Y, Erbaş O (2025). Antioxidant-effective quercetin through modulation of brain interleukin-13 mitigates autistic-like behaviors in the propionic acid-induced autism model in rats. J. Neuroimmune Pharmacol., 20: 1–16. https://doi.org/10.1007/s11481-025-10190-w

Kundu JK, Surh YJ (2008). Inflammation: Gearing the journey to cancer. Mutat. Res., 659: 15–30. https://doi.org/10.1016/j.mrrev.2008.03.002

Lagod PP, Naser SA (2023). The role of short-chain fatty acids and altered microbiota composition in autism spectrum disorder: A comprehensive literature review. Int. J. Mol. Sci., 24: 17432. https://doi.org/10.3390/ijms242417432

Liu F, Li J, Wu F, Zheng H, Peng Q, Zhou H (2019). Altered composition and function of intestinal microbiota in autism spectrum disorders: A systematic review. Transl. Psych., 9: 43. https://doi.org/10.1038/s41398-019-0389-6

Martinez-Micaelo N, González-Abuín N, Ardevol A, Pinent M, Blay MT (2012). Procyanidins and inflammation: Molecular targets and health implications. Biofactors., 38: 257–265. https://doi.org/10.1002/biof.1019

Metwally AM, Salah El-Din EM, Abdel Raouf ER, Elsaied A, Ashaat EA, Yousef W, El-Sonbaty M (2024). Ajwa dates reduce oxidative stress in egyptian children with autism: A six-month randomized controlled trial. Egypt J. Chem., 67: 585–599. https://doi.org/10.21608/ejchem.2024.329150.10649

Patterson ZR, Holahan MR (2012). Understanding the neuroinflammatory response following concussion to develop treatment strategies. Front. Cell Neurosci., 6: 58. https://doi.org/10.3389/fncel.2012.00058

Saeed A, Atshan SS, Jabbar L, Alkufi HK (2025). Rational use of antibiotics for community acquired pneumonia in Thi-Qar's Hospitals. J. Commun. Dis., 57: 2.

Shultz SR, MacFabe DF, Ossenkopp KP, Scratch S, Whelan J, Taylor R, Cain DP (2008). Intracerebroventricular injection of propionic acid, an enteric bacterial metabolic end-product, impairs social behavior in the rat: implications for an animal model of autism. Neuropharmacology, 54: 901–911. https://doi.org/10.1016/j.neuropharm.2008.01.013

Strandwitz P (2018). Neurotransmitter modulation by the gut microbiota. Brain Res., 1693: 128–133. https://doi.org/10.1016/j.brainres.2018.03.015

Tchaconas A, Adesman A (2013). Autism spectrum disorders: A pediatric overview and update. Curr. Opin. Pediatr., 25: 130–143. https://doi.org/10.1097/MOP.0b013e32835c2b70

Ukkirapandian K, Elumalai K, Udaykumar KP, Vp S, Rangasmy M, Ponnambalam S (2024). Behavioral and Biochemical Assays for Autism Models of Wistar Rats. Cureus., 16: e52066. https://doi.org/10.7759/cureus.52066

Vaughan CA (2011). Test review: E. Schopler, ME Van Bourgondien, GJ Wellman, and SR love childhood autism rating scale. Los Angeles, CA: Western Psychological Services, 2010. J. Psychoeduc. Assess., 29: 489–493. https://doi.org/10.1177/0734282911400873