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# Astounding the anxiolytic and eudemonic potential of certain fruits

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ABSTRACT

Anxiety is a state of mind with some fear that affects physical health by disrupting neurotransmission and hormonal control. Both diet (inadequate and unhealthy dietary patterns) and environment (social and financial factors) trigger its progression; therefore, diet is considered to have a significant involvement in its prevention or adjunct therapy. A unique nutrient profile and bioactive ingredients are seen in fruits to provide health outcomes beyond nutritive properties. The relaxing potential of such fruits is attributed to the functional nature and therapeutic ingredients ***i.e.,*** catecholamines, myricetin, quercetin, betalains, etc. that enhance the efficiency of hormones, neurotransmitters, and metabolic pathways. This review presented certain fruits having positive associations with mental health and anxiety amelioration. Various types of research evidenced the anxiolytic effect of certain fruits through clinical trials. Among them, berries, opuntia, and black pepper also have shown anxiety-relieving effects in clinical studies by restoring antioxidant enzymes, hormonal modulations, and managing neurotransmitters. Citrus species are loaded with flavonoids which are involved in the expression of GABA (Gamma-Amino Butyric Acid) to calm the nervous system. Some other fruits also potentiate memory and cognition when taken in ample amounts owing to their secondary metabolites. Thus, the incorporation of such fruits into a regular diet has been found to have a significant impact on mental well-being and brain health.

## 1. Introduction

Anxiety is a state of apprehension that something bad or unpleasant will occur. Significant impairment of social and physical functioning of the body differentiates anxiety from fear that one experiences normally in daily life. It is characterized by a high level of cortisol, a stress hormone, and the excitability of the nervous system. It is characterized by a rapid, strong, irregular heartbeat, and sweating [1,2]. According to an estimation, the global prevalence of anxiety in 2021 was recorded as up to 25.8 % among doctors due to the COVID-19 pandemic [3]. One meta-analysis of university students in Pakistan showed that the prevalence of depressive symptoms was 42.66 % [4]. And it is increasing day by day due to various factors including societal changes, challenging work environment, heightened stress, and pandemics like COVID. Generally, it is a normal human experience, but it can periodically become excessive and develop into a disorder. The instrumental activities of daily living (IADL), which include driving, cleaning, and handling finances, may be affected at this point [5]. Personal and professional facets of life suffer when these essential everyday tasks deteriorate. These people may have difficulty in hearing, remembering, concentrating, learning, and communicating. Self-care and mentalization get diminished due to poor understanding or less control over behaviour and accepting the change [6]. Additionally, comorbid conditions like depression, phobias, post-traumatic stress disorder,

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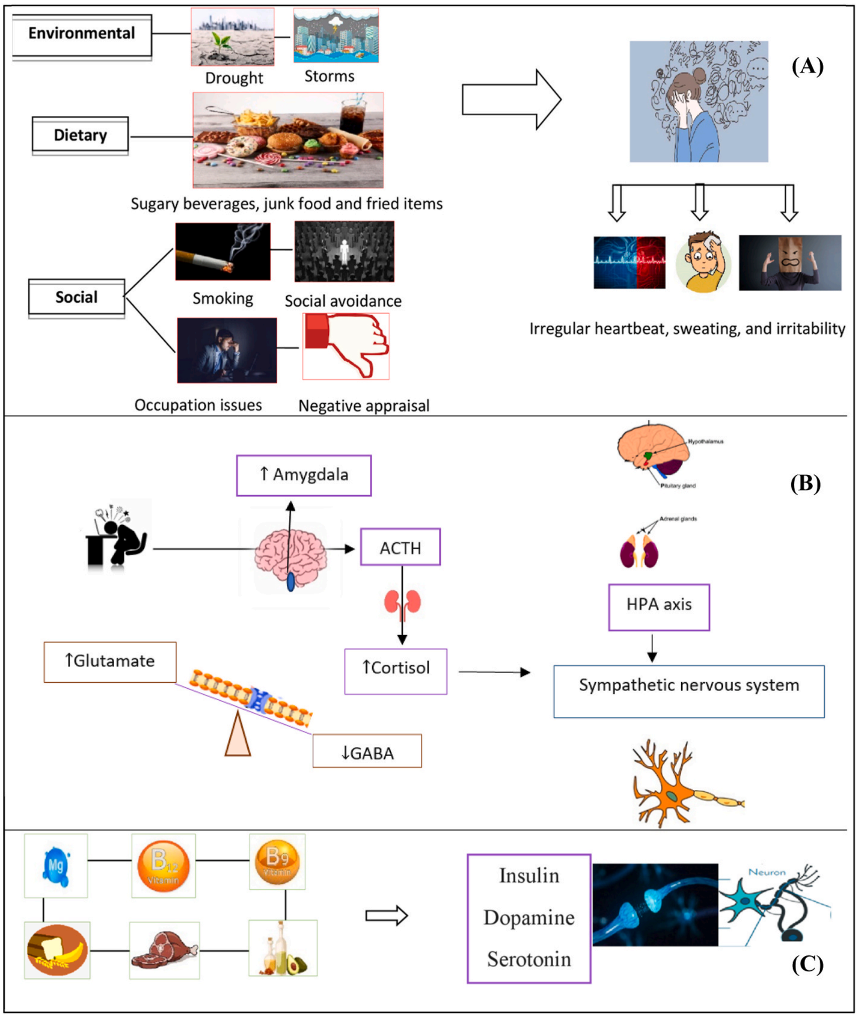


**Fig. 1.** (a) Risk factors of anxiety (b) Mechanism of anxiety (c) Nutritional basis of anxiety.

alcoholism, and drug addiction can accompany anxiety. The activities of daily living are hampered by these comorbidities, which also raise the risk of chronic illness, hospitalizations, and even suicide attempts [7]. Dietary, social, and environmental factors contribute to developing anxiety. These modifiable risk factors should be avoided to prevent serious issues. Junk food or processed items, including meat and meat products, are closely associated with anxiety. Sugary foods not only raise glycemic load but also induces stress and glycation, which is the primary cause of oxidation. Inadequate intake of food items or overconsumption of empty energy-dense foods should be avoided [8,9].

Social factors contributing to anxiety are cigarette smoking, avoidance of social gatherings, issues in an occupation that may be financial or moral, and negative appraisal of efforts raising the fear of incapability and insecurities about someone's skills. These can be modified by enhancing physical activity by walking, exercising, sports, or maintaining coping skills to participate in social gatherings. Social and moral support is the key to helping these factors that may originate anxiety 6 months or later [10].

Brain-derived neurotrophic factors maintain dopaminergic neurotransmission and are neuroprotective. Physical activity enhances this protein expression along with the enhancement of endorphins to prepare the body for stress management. Smoking enhances stress hormones, *i.e.,* cortisol. Smokers have a low resting period for beta-endorphins, stress managers in the pituitary glands. Long-term exposure activates the HPA (hypothalamus, pituitary glands, and adrenal glands) axis leading to an anxious state by enhancing stress hormones [11–13]. Negative emotions arising from environmental problems, *i.e.,* climate and survival issues, lead to negative well-being. Personality factors greatly affect response patterns to stress [14]. Fig. 1 (a) describes the risk factors which are associated with anxiety.

Amygdala comes from the Greek word meaning almond, located in the temporal lobe, anterior to the hippocampus and is responsible for processing emotions and memory [15]. It responds to fear and anxiety through hyper-activation [16]. Gamma-aminobutyric acid (GABA) is a neurotransmission center for primary inhibition in the central nervous system. It functions to reduce neuronal excitability by inhibiting the nerve transmission of neurons. GABAergic neurons are present in the hippocampus, thalamus, hypothalamus, and brainstem. It works in a counterbalance mechanism with the excitatory neurotransmitter, i.e., glutamate and the inhibitory neurotransmitter GABA to calm the brain [1]. Stress stimulates the HPA axis to activate the release of glucocorticoid hormone to initiate sympathetic nervous retorts. The cerebral cortex stimulates the hypothalamus to release corticotropin-releasing hormone (CRH), which stimulates the pituitary gland to produce and release adrenocorticotropic hormone (ACTH). ACTH then directs adrenal glands to synthesize and release cortisol. These modulations compensate for energy requirements by regulating energy metabolism. Over-stimulation of these pathways exerts harmful effects on the nervous system [17]. The mechanism of anxiety is presented in Fig. 1 (b).

Anxiety has a psychological, physiological, and nutritional basis. Therefore, nutrition significantly impacts the induction and progression of anxiety. Nutrients play a key role in hormone release and the normal functioning of neurotransmitters. Macronutrients are the major constituents of food. Among them, carbohydrates trigger insulin release proteins, a source of tryptophan and tyrosine, which are precursors to mood-stabilizing hormones, and fats (especially polyunsaturated fatty acids) make up 50 % of grey matter in the brain. Vitamins and minerals are also responsible for neurotransmission, cognition, cellular development, and signaling pathways. Beyond macronutrients and micronutrients in food, some bioactive compounds are also derived from plants that modulate hormonal and neurotransmitter release by interacting with their pathways [18,19]. The interrelation between food and anxiety is shown in Fig. 1(c).

Fruits are edible parts of plants consisting of seeds and surrounding tissues and these possess nutritive and medicinal value, excellent flavor, and attractive colors [20–22]. Depending upon their origin and temperature, fruits are classified into three categories: temperate, sub-tropical, and tropical [23,24]. Pigments in them, such as carotenoids, flavonoids, and anthocyanidins, determine their color [25,26]. These are secondary metabolites with potent antioxidant power [27]. They are enriched with micronutrients and are positively linked with gut and mental health [28,29]. They are largely consumed throughout the world due to their nutritive and phytochemical nature, making them effective for medicinal use. Their anti-diabetic, anti-cancer, anti-hypertensive, neuroprotective, immunomodulatory, and anti-convulsant abilities make them therapeutic beyond basic nutrition [30,31]. They have a key role in preventing heart diseases and gastrointestinal disorders. Their bioactive profile including various phenolic acids (gallic acid, caffeic acid, and ellagic acid) may also reduce the risk of certain types of cancer [32,33][34]. Other abnormalities, including age-related macular degeneration, eye cataracts, skin conditions, lipid profile, cholesterol, and immune function, are associated with consuming fruits [35,36]. Therefore, there is a need to evaluate such fruits and utilize them for certain health issues. Although daily consumption of fruits is key to an adequate diet. United States Department Agriculture (USDA) recommends filling up a quarter plate with fruits because they provide a good amount of dietary fiber, certain vitamins (e.g., ascorbic acid, folic acid, and vitamin A precursors), many minerals (e.g., potassium, magnesium, iron, and calcium), and many other important phytochemicals with strong antioxidative properties. While ingesting an ample amount might exert medicinal effects. Various studies conducted on fruits functioning as anxiety relievers are needed to have practical insights to illustrate the findings of clinical research. The presented review summarizes the general bioactive profile along with their impact on anxiety with evidenced clinical results to ensure their practical implications for therapeutic purposes. Moreover, a novel method explains the mechanism behind the anxiolytic effect.

## 2. Anxiolytic effects of fruits

Fruits play a vital role in human health and metabolism. Besides having essential vitamins and minerals, they are loaded with antioxidant, and antibacterial substances to provide health benefits beyond basic nutrition. The pigments are associated with lowering the occurrence of various diseases e.g., anthocyanins are associated with reduction of cardiovascular disorders [37,38]. Here are some fruits that have been found to help alleviate anxiety based on clinical trials conducted in the past five years.

### *2.1. Berries*

Berries are small fleshy fruits with an ovary wall growing into the fruit's flesh, and the seeds are enclosed in a jelly-like pectinaceous matrix [39]. They are rich in vitamin C, a potent antioxidant, and vitamins E and B. Its phytoconstituents are phenolic compounds, including flavonoids, tannins, and phenolic acids. Besides nutrition, they are also renowned in medicinal therapy for diabetes, cardiovascular problems, and other diseases due to polyphenols, such as blackberries, blackcurrants, blueberries, strawberries, etc. [40]. Polyphenols are positively associated with mental health. They are processed into metabolites such as short-chain fatty acids (SCFA) and behave as neurotransmitters as they can indirectly cross the blood-brain barrier to modulate the cerebrovascular system. The bidirectional system of gut hormones and the nervous system is referred to as the microbiota-gut-brain axis, which plays a key role in stress responses. Metabolites in the gut have the ability to modulate microbiota and brain physiology [41]. Gut microbiota communicates with nerves via the vagus nerve, cell wall, metabolites, neurotransmitters, and brain neurotrophic factors. They can also synthesize neurotransmitters such as GABA [42].

#### *2.1.1. Banana*

Bananas belong to the genus *Musa* and the family Musaceae [23]. They have valuable ingredients such as vitamins, polyphenols, steroids, triterpenes, phytosterols, biogenic amines, phenolics, and carotenoids. They also possess biological activities such as antidiarrheal, anti-ulcerative, anti-microbial, antioxidant, hypoglycemic, wound healing, and anti-cancer activity [43]. Bananas are rich in essential phytonutrients, such as phenolic compounds and vitamins ($B_3$, $B_6$, $B_{12}$, C, and E). Its pulp is rich in vitamin $B_6$ which is potentially active in improving mental health. Additionally, it includes dietary fiber, carotenoids, flavonoids, and amine chemicals. Indigestible carbohydrate polymers such as dietary fiber are also present as soluble and insoluble fiber in them [44]. According to reports, banana peel extract (BPE) typically contains more dietary fiber than banana peel [45].

An experimental study with a pretest-posttest control group design was carried out using 60 participants, and they were given bananas on a daily basis. The Hamilton Anxiety Rating Scale (HARS) was used to gauge the level of anxiety. Anxiety post-test scores were measured seven and fourteen days following the intervention. There was a reduction in anxiousness. After the intervention, the intervention group possessed a significantly lower anxiety level than the control group ($p < 0.05$) [46]. Likewise, a study in which BPE (400 mg/kg; oral administration) provision to the test group for 14 days was performed by Samad et al. [47]. For depression/anxiety-like behaviour, the elevated-plus maze, the forced-swim test, and light-dark activity box tests were used, respectively. The Morris water navigation task was used to evaluate memory. Animals were sacrificed after behavioral tests, and the brain was removed for biochemical analysis and histological research. In the current investigation, BPE improved memory and had anxiolytic and antidepressant-like effects. In animals treated with BPE, antioxidant enzyme activity increased while AChE and MDA levels dropped. BPE also restored normalcy to histopathological changes brought on by noise stress. Thus, it has been determined that banana peel supplementation or administration has protective benefits against anxiety, depression, and memory impairment.

*2.1.1.1. Anxiolytic mechanism.* Bananas comprise antioxidant vitamins such as vitamins A, C, and E. They prevent oxidation by suppressing the formation of reactive oxygen species, reducing hydroperoxides, stimulating the activity of antioxidant enzymes, or repairing oxidative damage. Catecholamines, *i.e.,* tryptophan, are a precursor of serotonin, a happy hormone [48]. Besides increasing serotonin and tryptophan to calm the body, they are also rich sources of zinc and magnesium making them effective in improving mental health. Carbohydrates in them stimulate the release of insulin to take up glucose for bodily activities. Insulin further initiates the synthesis of a hormone and neurotransmitter, *i.e.,* serotonin. The activity of antioxidant enzymes is also

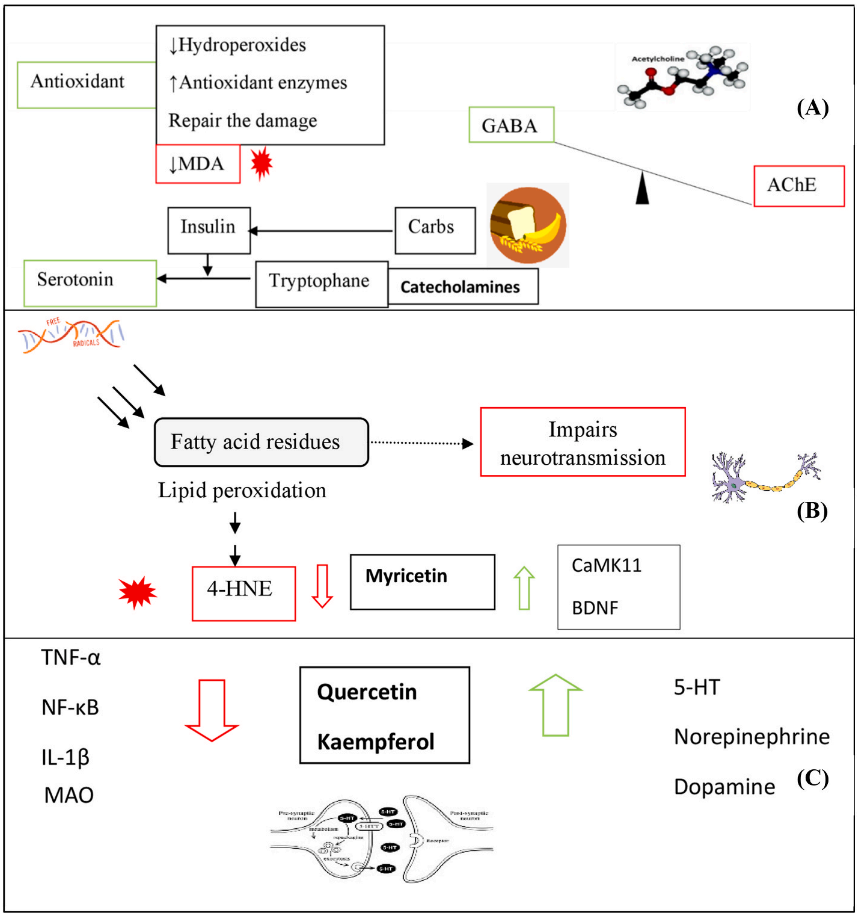


**Fig. 2.** The anxiolytic effect of (a) Banana (b) Blueberry and (c) Grewia.

increased while levels of acetylcholinesterase or AChE and malondialdehyde or MDA are reduced after BPE treatment [47,49], as shown in Fig. 2 (a).

*2.1.2. Blueberry*

Blueberries originate from the genus *Vaccinium* L., the richest source of phytonutrients. They have antioxidants, and metabolites for their effectiveness in preventing numerous degenerative diseases [50]. They improve cognition by modulating blood circulation and neurotransmission [51]. Their regular intake reduces the rate of cardiovascular diseases and diabetes. They also aid in weight maintenance due to their low caloric and nutrient-dense profile. One of its aspects is vaso-modulation and glucose control. Its anti-inflammatory and antioxidant status makes it a superfruit [52].

Krishna et al. [53] performed a study in which, rats were kept on a blueberry-supplemented diet (5 % w/w) for two weeks after traumatic brain injury which helped to lessen the effects of the injury on anxious behaviour as well as the loss of spatial learning and memory. The effects of the brain-derived neurotrophic factor (BDNF) system on learning and memory are mediated by molecules such as cAMP response element binding factor (CREB), and $Ca^{2+}$/Calmodulin-dependent protein kinase II. A significant decrease in BDNF and CaMKII was observed. A rise in the lipid peroxidation byproduct 4-hydroxy-nominal (4-HNE) was also reversed. Another study by Sinclair et al. [54] sought to determine the effects of tart cherry and blueberry juices on cardiometabolic and other health indices. 45 adults were divided into three groups at random and given 60 mL of tart cherry, blueberry, or a placebo to drink every day for 20 days. Blueberry arm outperformed the placebo statistically in psychological health indicators assessed by the Beck Depression Scale, State-Trait Anxiety Inventory, and COOP WONCA which showed significant improvement. This research suggests that it could be a useful strategy to help manage psychological wellness to health-related quality of life.

*2.1.2.1. Anxiolytic mechanism.* Myricetin is present in blueberries and responsible for their antioxidant status [55]. It is a general flavonoid exhibiting various pharmacological activities, including HPA axis regulation, that forms the basis of anxiety. It normalizes the increase in cortistatin and adrenocorticotropic hormone levels initiated by HPA axis dysfunction. This dysregulation is due to an imbalance of 5-HT receptors, which function to excite the motor ability of neurons [56]. One of the secondary products, 4-HNE, is a by-product of lipid peroxidation occurring in neurons due to oxidation induced by stress. This induces the release of pro-inflammatory cytokines to exhibit inflammation. Anthocyanins inhibit the ionic and signaling disruption caused by their elevation. It diminishes the level of 4-HNE; otherwise, it will cause damage to the brain region as this chemical is responsible for spatial memory and behavioral performances [57,58]. CaMK11 and brain-derived neurotropic factors are the nervous system molecules associated with cognition and performance, as they are central to synapse formation and instruction managers for protein synthesis in the brain, respectively. In an anxious state, they may get depleted. Polyphenols in fruit extract have shown a potential effect on their restoration and maintenance, as shown in Fig. 2 (b) [59].

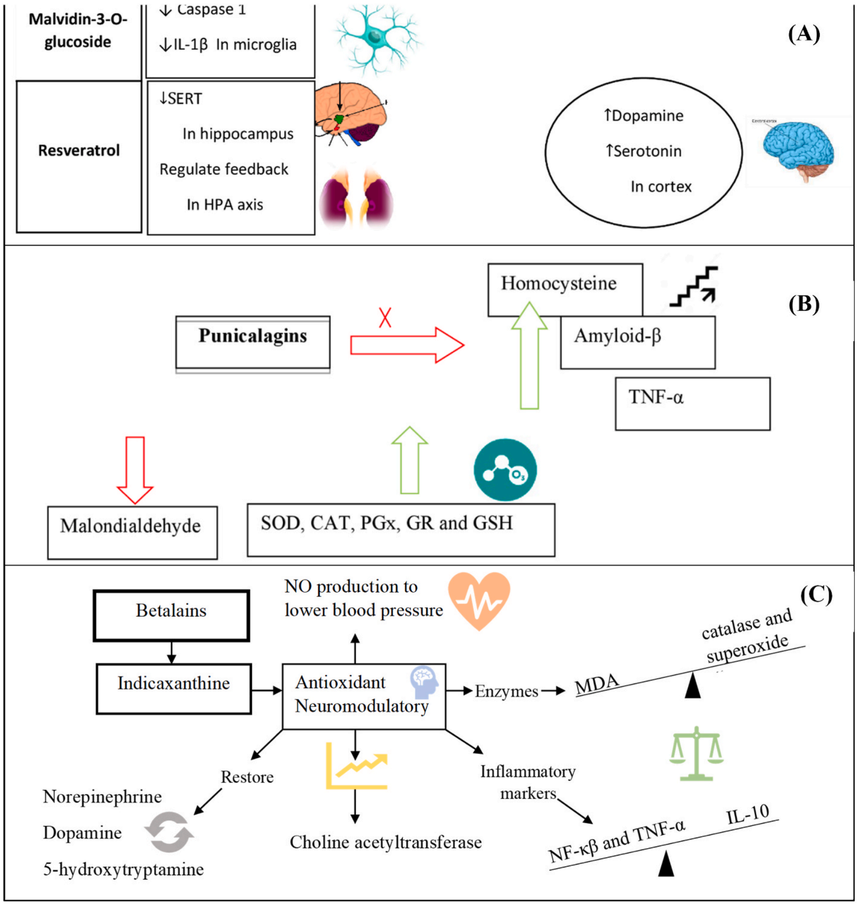


**Fig. 3.** The anxiolytic effect of (a) grapes (b) pomegranate (c) opuntia.

### 2.1.3. *Grewia*

*Grewia asiatica* L. belongs to the Malvaceae family. It is commonly known as phalsa for its conventional use as Rasayana. It is recognized for its stimulant potential and remarkable amending effect on cognition [60]. They possess multiple health outcomes due to their phytochemical nature. When consistently ingested, they are one of the best sources of bioactive food components with a variety of health advantages. Its fruit, seeds, and pulp are full of therapeutic compounds that can heal a wide range of illnesses and improve respiratory and cardiac functioning [61].

A study used an elevated plus maze model to test the cognitive enhancing ability of phalsa extracts (200 mg/kg) against scopolamine-induced amnesia. *G. asiatica*'s contents were determined in rat brains using spectrophotometric analysis, and histopathological studies were carried out to evaluate damages on AChE, lipid peroxidase, and SOD. Results revealed that methanolic extract of phalsa improved oxidative stress indicators, restored damaged cytoarchitecture of neurons, and modulated monoamines' influence on behaviour, making it a promising candidate for a nootropic. This restoration of memory caused by scopolamine-induced amnesia was measured on behavioral paradigms [62]. In another experiment, chronically fed rats were given different dilutions (5–30 %) of fruit juice before being evaluated behaviorally for anxiety, depression, and cognition (spatial memory) and then isolated brains were subjected to biochemical analysis. The open field test and open arms of the elevated plus maze demonstrated that treated animals exhibited anxiolytic behaviour to the central zone ($p < 0.05$) and 30 % dilutions of fruit exudate ($p < 0.05$), respectively, in anxiety models. Exudate treatment often reduced immobility in rats during the forced swim test (FST), exhibiting antidepressant-like effects ($p < 0.05$) [63].

#### 2.1.3.1. *Anxiolytic mechanism.*

Among flavonoids, quercetin and kaempferol are responsible for black currants' anti-inflammatory, anti-oxidant, and anti-anxiety potential. They have been shown to prevent the release of pro-inflammatory cytokines (TNF-α, NF-κB, and IL-1β) from microglia cells in the brain region [64]. The hyperactivity of monoamine oxidase A (MAO-A) is a well-known stress response involved in the central 5-HT or serotonergic system [65]. One of its pathways to reduce anxiety is enhancing the availability of serotonin. Inhibition of monoamine oxidase (MAO) activity in synapses facilitates the serotonin level in the synaptic region [66]. Because monoamine oxidase breaks neurotransmitters, *i.e.,* serotonin. 5-HT neuronal activity is enhanced in stress. Both have also been reported to upregulate neurotransmitters that are relaxants for the nervous system. Norepinephrine and dopamine are enhanced in the brain to provide a calming effect due to up-regulation, as seen in Fig. 2 (c) [67].

### 2.1.4. *Grapes*

Grapes belong to the Vitis family with extensive antioxidant potential [68]. Constitutive bioactive molecules in these fruits are phenolic acids, anthocyanins, flavonoids, lipids, lycopene, and stilbenes. They are consumed in the form of grape juice, raw, or extracts for healthy outcomes for various diseases owing to their antioxidant potential [69,70]. Their functionality is attributed to their phytochemicals in leaves and pulp that have shown great impact on cure and prevention by exhibiting anti-inflammatory, anti-diabetic, hepatoprotective effect, anti-hypertensive, cardioprotective, and anti-microbial via in-vitro and in-vivo studies [71,72]. In an investigative study using female mice, behavioral experiments and high throughput genome-wide RNA transcriptome studies were used to examine the impact of dietary grape consumption. By adding 1 % grape powder to the high fructose diet. Anxiety-like behaviour was assessed by using an open-field test which indicated a significant reduction in anxiousness [73]. Paulet, Ciobica [74] were concerned about the effects of 300 mg/kg grape pomace extract in terms of cognition. He administered the extract for three days and assessed spatial memory, potential locomotor activity, and anxiety behaviour. According to the behavioral changes seen in the raised plus maze test, it was concluded that grape pomace is effective in behavioral improvement and better cognition.

*2.1.4.1. Anxiolytic mechanism.* A subclass of anthocyanin, *i.e.,* malvidin-3-*O*-glucoside (MG) is present in high proportions in grapes. It significantly reduces caspase-1 and IL-1β protein levels in microglia, accounting for 10–15 % of brain and spinal cord cells. In a study, MG has shown the best anti-inflammatory potential among 13 polyphenols. Hyperactivation of adrenal glands with increased corticotropin-releasing factor (CRF) and glucocorticoid receptor (GR) in the hypothalamus, hippocampus, and amygdala was observed in an anxious state. Resveratrol reversed their upregulation and restored the feedback mechanism for their regulation in the HPA axis that was overactivated after a traumatic event [75,76]. These three brain regions (hypothalamus, hippocampus, and amygdala) are concerned with HPA-axis dysfunction linked to anxiety and memory deficits [77]. In the cortex region of the brain, dopamine and serotonin are raised by decreasing the serotonin transporters, which are present in the hippocampus, as seen in Fig. 3 (a) [78,79].

### 2.1.5. Pomegranate

Pomegranate (*Punica granatum*) is anciently known for its phytochemical nature. Besides phenolic and aromatic compounds, tocopherols, amino acids, terpenoids, alkaloids, indoleamine, etc., are also present in their chemical profile [80]. Ellagitannins (including punicalagin), ellagic acid, flavonoids, estrogenic flavones, anthocyanidins, punicic acid, and anthocyanins are major constituents with distinctive potentials. It presented bone-protective, anti-diabetic, anti-hypertensive, hepatoprotective, and neuroprotective properties. The immune system is also mediated by its bioactive substances and their impact on cognition and behaviour [81–83].

Fathy et al. [84] conducted an experiment in which three of the four groups of mice received paraquat (10 mg/kg) in two days of a week for three weeks. Pomegranate seed extract and pomegranate juice were administered and tested for phytochemicals, total phenolics, and total flavonoids. Tyrosine hydroxylase (TH), striatal dopamine (DA), 3, 4-dihydroxyphenylacetic acid (DOPAC), the striatum's levels of ATP, malondialdehyde, and the action of antioxidant enzymes were calculated. Therefore, oxidation was reduced induced by neuroinflammation suggesting the neuroprotective potential of pomegranate [85].

*2.1.5.1. Anxiolytic mechanism.* Punicalagin, its major ingredient, is a natural polyphenolic compound classified as ellagitannin. They have potent antioxidant power with 50 % antioxidant capacity and anti-inflammatory effects [82]. They significantly prohibited the rise in amyloid-β, homocysteine, and TNF-α. Homocysteine is a sulfur-containing molecule with an amino acid profile. It is strongly excitatory in its action and may have a toxic impact when overstimulated. While amyloid-β is a damage marker in brain physiology. These tannins are associated with an increase in the activities of antioxidant enzymes such as superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (PGx), glutathione reductase (GR), and glutathione (GSH) levels [86,87]. Oxidative damage caused by malondialdehyde is another cause of oxidative stress that is subsequently downregulated, as shown in Fig. 3 (b) [88].

### 2.1.6. Opuntia

*Opuntia* belongs to the cactus family and is an acidic fruit with a high quantity of vitamin C, betalains, tannins, phenols, and flavonoids. *Opuntia ficus,* also known as prickly pear, is renowned for its biological activities attributed to nutraceuticals. It is loaded with flavonoids such as quercetin, isorhamnetin, indicaxanthin, and vitamins A, C, E, and $B_1$. It [89]. This is derived from desserts with delicious taste and medicinal properties regarding human health. It is commonly known as cactus fruits or prickly pears. These are oval-shaped berries with glochids covering a juicy pulp inside with a sweet flavor. Its higher content of vitamin C makes it a potent antioxidant. It is rich in micronutrients, especially calcium and magnesium. It has a health-promoting effect on bones, the cardiovascular system, kidneys, and the gastrointestinal tract. It is therapeutic for its antioxidant, antibacterial, anti-inflammatory, hepatoprotective, gastroprotective, anti-inflammatory, neuroprotective, sedative, pain-relieving, anxiolytic, and anti-microbial properties [90–92].

Akkol et al. [93] conducted a study to identify the components responsible for the activity and to experimentally confirm the effectiveness of the fruits of *Opuntia ficus indica*. Five sub-extracts were created by sequentially fractionating the fruits' crude methanolic extract. Each extract was subjected to bioassay systems for activity evaluation; traction, fireside, elevated plus-maze, and open-field tests were used to measure sedative and antianxiety effects, respectively, and a thiopental-induced sleeping assessment was utilized to analyze hypnotic effects. In conclusion, this investigation supported this Turkish traditional medicinal plant to treat anxiety as significant hypnotic and sedative effects were observed.

*2.1.6.1. Anxiolytic mechanism.* The extract of opuntia has shown the highest concentration of betanin, a sub-class of phenolic compounds. They have recently been gaining attention in scientific interest due to their high levels of bioactive phytochemical compounds, particularly betalains. One of its types is indicaxanthine which is bioavailable to the human body and exerts antioxidant and neuromodulatory effects in the body. It has been proven to cause vasodilation and nitric oxide production to lower blood pressure that has been raised due to the sympathetic nervous system [94]. Besides scavenging free radicals, it also enhances the expression of genes associated with antioxidant pathways [95]. There was a significant decrease in pro-inflammatory cytokines (NF-κβ and TNF-α) and a remarkable increase in anti-inflammatory cytokine (IL-10). Monoamine neurotransmitters such as norepinephrine, dopamine, and 5-hydroxytryptamine which are basic regulators of memory and cognition, are also restored. Their deficiency in the hippocampus causes cerebral damage leading to neuropsychiatric disorders. Acetylcholinesterase level (AChE) is increased in the anxious state, which is subsequently adjusted to normal by phytochemicals. Association with SERT was also seen in a study [96]. An experiment increased antioxidant enzyme activities in the brain, such as catalase and superoxide dismutase activity, as well as a reduction in MDA levels. It also managed to increase the activity of choline acetyltransferase in cholinergic neurons involved in the formation of acetylcholine, as shown in Fig. 3 (c) [97].

### 2.1.7. Passion fruit

*Passiflora edulis* is conventionally named Krishna Phal in India. It belongs to Passifloraceae, the largest family of passion fruits with multiple therapeutic properties. It is well known for its anti-diabetic, anxiolytic, anti-tumor, antioxidant, analgesic, and anti-inflammatory activities. Its pharmacological potential is attributed to its major constituents such as flavonoids, triterpenoids, aldehydes, ketones, tridecanone, palmitic acid, stearic Acid, linoleic Acid, quercetic, apigenin, and vitexin [98,99].

In an experiment, behaviour tests were conducted 60 min after the treatments on Swiss mice divided into four groups and given doses of

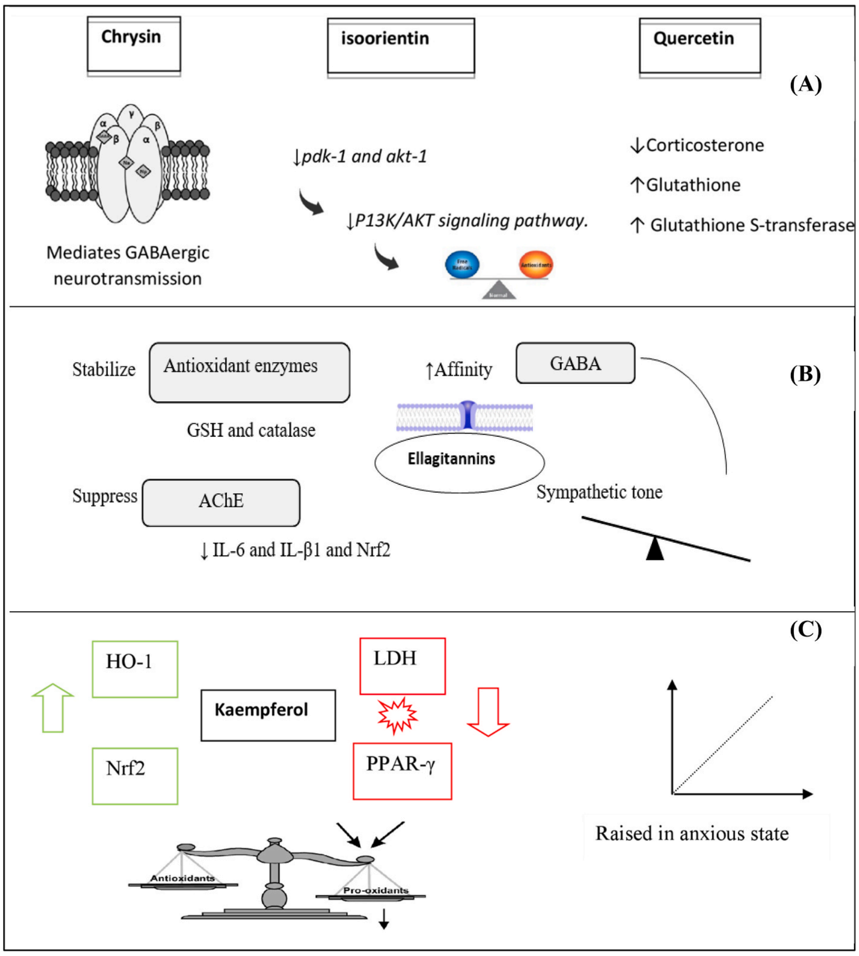


**Fig. 4.** The anxiolytic effect of (a) passion fruit (b) blackberry and (c) strawberry.

passion fruit (200 or 400 mg/kg body weight), water, and diazepam (as a -ve and +ve control). *P. tenuifila* fruit treatment significantly reduced locomotor activity in the rats, indicating sedative and anxiolytic effects. It had a protective effect in contradiction to pentylenetetrazole-induced seizures, lessening their severity and preventing the animals from dying. The flavonoids and phenolic acids in *P. tenuifila* may have contributed to its potential as an anxiolytic, hypnotic-sedative, and anticonvulsant drug because it exhibited little acute toxicity [100].

*2.1.7.1. Anxiolytic mechanism.* Polyphenol chrysin belongs to a class of flavonoids obtained from passion fruit. It mediates receptors for GABAergic neurotransmission [101]. Fruit pulp is a rich source of flavonoids *i.e.,* isoorientin [102] and quercetin [103]. Isoorientin decreased pdk-1 and akt-1 expression in mRNA, thus downregulating the P13K/AKT signaling pathway. This pathway maintains a redox balance [104,105]. In a study conducted in 2021, quercetin decreased the level of stress-related corticosterone and maintained glutathione and glutathione S-transferase for oxidation homeostasis, as seen in Fig. 4 (a) [106].

### 2.2. *Aggregate fruit*

Some fruits are derived from a single flower containing many ovaries inside. Several ovaries and flowering bodies are combined into one fruit component which has been categorized as aggregate fruits [107,108]. Blackberries are considered aggregate fruits due to their ripening stages as well. They change from green to red and then completely purple with the full-ripened stage [109].

#### 2.2.1. *Blackberry*

Blackberries belong to the Rubus family, the richest source of ellagitannins, flavonols, anthocyanins, tannins, and flavonoids. They positively affect the gastrointestinal tract via the mediating gut microbiota. Gut-brain axis modulation is positively attributed to berries. They have protective roles in preventing chronic disease states [110–112]. Blackberries are rich in anthocyanins, a subclass of flavonoids and secondary metabolites. These compounds offer several health benefits such as antioxidants, anti-microbial, anti-cancer, and antipyretic. Besides anthocyanins, ellagitannins are present for their cardioprotective activity [113,114].

In a study conducted by Fernandez-Demeneghi et al. [115], the effects of blackberry juice on anxiety-like behaviour in Wistar rats were assessed. The juice was rich in various concentrations of anthocyanins and polyphenols. The elevated plus maze, locomotor activity test, and forced swim test were performed on the rats after blackberry juice treatment for 21 days. The intermediate dose of blackberry juice had a diazepam-like anxiolytic effect without impairing motor activity and decreased total immobility time in the forced swim test, indicating a protective effect against behavioral alterations brought on by acute stress. These results point to a potential therapeutic benefit of blackberry juice in treating anxiety brought on by stressful events.

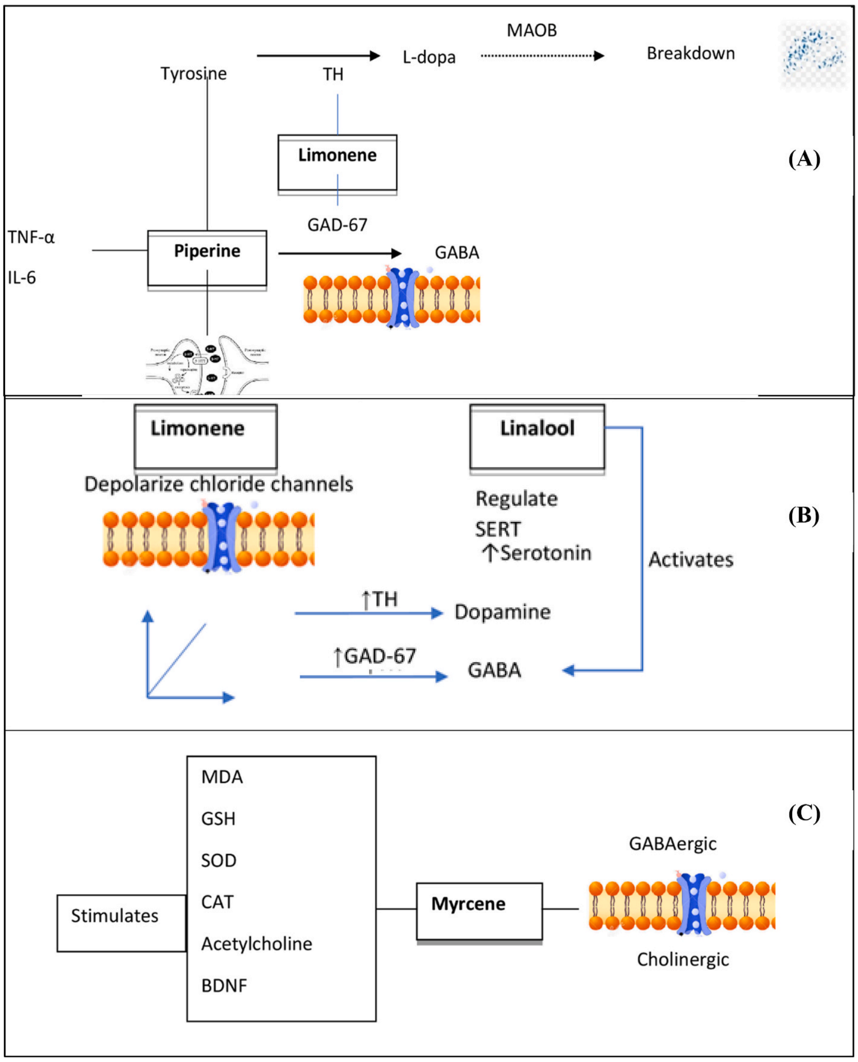


**Fig. 5.** The anxiolytic effect of (a) black pepper (b) bitter orange and (c) sweet lime. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

*2.2.1.1. Anxiolytic mechanism.* Ellagitannins in fruit extract function at enzymatic, inflammatory and neurotransmission levels to cope with anxiety. They restore the level of glutathione and catalase to prevent inflammation, as these are antioxidant enzymes. Acetylcholine prevents the excessive firing of neurons in stress conditions. But this neurotransmitter is quickly broken down by a serine hydroxylase enzyme named acetylcholinesterase. This hormone is inhibited, which adjusts anxiety's excitatory tone to a normal level [116,117]. Polyphenols augment GABAergic neurons by increasing their affinity to their receptors to inhibit neurotransmission. Protecting the activity of GABA is a key modulator of stress. GABA responds to stress to relax the nervous system and switch to a parasympathetic tone [118]. Regulation of pro-inflammatory substances is attributed to the ellagic acid present in berries. They regulate the pathways of IL-6 and IL-β1 and Nrf2, which are associated with inflammation. Reducing inflammation is the first-line response to stress stimuli described in Fig. 4 (b) [119].

### 2.2.2. Strawberry

*Fragaria ananassa*, commonly termed strawberry, contains flavonoids, anthocyanins, and derivatives of ellagic and hydroxycinnamic acids. It comprises large amounts of dietary fiber, fatty acids, and other substances, including nutrients like minerals, vitamins like ascorbic acid, folate, and essential oils, with strong antioxidant effects [120,121]. These substances impact allergies, inflammation, obesity, wound healing, platelet aggregation, hypertension, melanogenesis, nephropathy, and bacterial infections. Additionally, regular intake helps prevent certain chronic illnesses like dementia, Alzheimer's disease, and cardiovascular problems [122,123].

In an experimental study, female Wistar rats were pretreated orally with fresh, simmered, and frozen methanolic extracts (250 mg/kg) of strawberry for two weeks. The fresh extract improved anxiety and perceptive dysfunction, elevated biomarkers such as HO-1 and $Nrf_2$ value, and significantly decreased caspase-3 and PPAR levels when compared to cooked and frozen extracts. $Nrf_2$, PPAR and LDH were downregulated. In summary, the fresh extract has neuroprotective properties that show promise for reducing age-related neurodegeneration [124].

*2.2.2.1. Anxiolytic mechanism.* The anxiolytic activity diminished the level of LDH or lactate dehydrogenase enzyme. Its extracellular activity is raised as a marker of damage. Thus, it is raised in the body when glutamine is increased as an indicator of stress. The antioxidant potential of strawberries is greatly attributed to kaempferol [125]. Another enzyme involved in preventing oxidation is HO-1 or heme oxygenase, which is responsible for heme transport and degradation and affects neuronal signaling pathways by generating carbon monoxide after splitting up heme iron. It is an antioxidant enzyme that works for neuronal defense, and protects neurons from oxidation, and cells from $H_2O_2$-induced death. $H_2O_2$ is pro-inflammatory and acts as a messenger in extracellular space. $Nrf_2$ levels are also restored to regulate inflammation as they regulate cellular resistance to oxidation. The literature has also shown a marked reduction in PPAR-γ levels as they are indicators of anxiety development in brain regions, as seen in Fig. 4 (c) [124].

### 2.3. *Drupe fruit*

Black peppers are single-seeded drupes or stone fruits in mature form. The pepper fruit is a single-seeded drupe, sometimes known as a berry. On a stalk, these berries are arranged in a helical pattern. The pepper berry is typically tiny, globular, and has a firm endocarp and a fleshy pericarp [126,127].

#### 2.3.1. *Black pepper*

Piper nigrum belongs to the Piperaceae family and possesses various pharmacological activities. Its dried form is named black pepper, commonly used as a spice for cooking purposes [128]. It is famous for its pungency and flavor and is called the king of spices. It has apparent antibacterial potential. It has been conventionally used as a therapeutic against foodborne pathogens and diabetes [129,130][131].

Experimental investigation about how methanolic extracts of *Piper nigrum* fruits (MEPNF), *Sesamum indicum* seeds (MESIS), and their combinations affect clot lysis in vitro thrombolytic activity were done by Emon et al. [132]. The Elevated Plus Maze test was utilized to assess the in vivo anxiolytic activity of diazepam (1 mg/kg) serving as a reference medication. The anxiolytic action of MEPNF and MESIS was considerable ($p = 0.001$) and dose-dependent. The frequency of time in the open arms and the frequency of entries have risen since MEPNF or MESIS 200 and 400 (mg/kg) were administered. In another experiment, an elevated plus maze (EPM) was used to assess the anxiolytic activity of black pepper essential oil, and the tail suspension test (TST) on mice was used to assess the antidepressant effect. To determine the potential mechanism of action, researchers used flumazenil, a competitive drug inhibiting the GABAA receptor in the benzodiazepine site. The animals were put through an open field test to weed out false-positive results brought on by increased locomotor activity (OFT). According to the study's data, oral acute and recurrent treatments with black pepper led to dose-dependent anxiolytic and antidepressant-like effects in EPM and TST, respectively. Flumazenil, but not WAY-100635, was able to counteract the effects of essential oil in both the EPM and TST, suggesting a potential role for the 5-HT1A receptor. The results imply that Piper nigrum EO, maybe through the involvement of serotonergic transmission, has a combined anxiolytic and antidepressant action [133].

*2.3.1.1. Anxiolytic mechanism.* Its pharmacological potential is attributed to its alkaloid *i.e.,* piperine. It is a central nervous system stimulant thus involved in neuropsychological issues [66,134]. Black pepper fruit has been shown to exhibit anxiolytic potential via the involvement of the 5-HT receptor in the serotonergic pathway [135]. It increased dopamine and tyrosine hydroxylase. Downregulation of MAOB and suppression of the release of TNF-α and IL-6 mediate anxiolytic activity. GABA and serotonin are raised in the cortical regions, thus altering the synaptic transmission [136]. Limonene present in it is a terpene commonly extracted from citrus species. It regulates dopamine synthesis via increasing the expression of tyrosine hydroxylase, a key enzyme involved in the formation of L-dopa from tyrosine in the catalytic reactions. The synthesis of inhibitory neurotransmitters, *i.e.,* GABA, is also regulated by glutamate decarboxylase 67 (GAD-67), as shown in Fig. 5 (a) [137].

### 2.4. *Citrus fruits*

Citrus family, Rutaceae, along with fruits, flowers, and leaves, are packed with secondary metabolites such as flavonoids, limonoids, carotenoids, coumarins, glutamates, anthocyanins, and phenolic acids. The economically important species are sweet orange, sour orange, lime mandarins, lemon, and grapefruit etc. Their non-nutritive compounds play vital role in smooth functioning of metabolic processes [138,139]. They have been credited with many biological potentials such as antioxidant, anti-cancer, anti-inflammatory, hypolipidemic, anti-hypertensive, anti-atherosclerotic, antithrombotic, anti-ulcer, antiallergy, and anti-microbial actions. Researchers also explored their association with the nervous systems such as anxiolytic, sedative, antidepressant, anticonvulsant, memory enhancing, and neuroprotective activities [140,141].

#### 2.4.1. *Bitter orange*

*Citrus aurantium* belongs to the Citrus family rich in carotenoids, flavonoids, terpenes, limonoids, and polymethoxylated flavones (PMFs), unique flavonoids, in citrus fruits exhibiting medicinal potential [142]. They are involved in antioxidant, anti-microbial, and metabolic pathways to improve their functioning [143]. Its peel is rich in *p*-synephrine and abundant flavonoids [144]. This delicious fruit is associated with satisfying hunger and managing blood glucose uptake and triglycerides level [145]. Their peels are also utilized in food industry as functional ingredients [146].

In a study held by Abdollahi and Mobadery [147], 60 patients with type 2 diabetes were randomly divided into two groups: the intervention group got bitter orange (*Citrus aurantium*) extract inhalation aromatherapy for three nights straight before sleeping, whereas the control group received standard treatment. Using a visual analogue scale, levels of weariness and anxiety were measured before and after the intervention (VAS). Before and after the intervention, the control group's patients' mean anxiety scores were $56.73 \pm 39.52$ and $56.6 \pm 3.93$, respectively ($p = 0.468$).

*2.4.1.1. Anxiolytic mechanism.* Limonene and linalool are the main ingredients that are anxiolytic. These are monoterpenes. Limonene initiates the depolarization of chloride channels and, subsequently, GABA release for inhibitory tone. The synthesis of GABA is mediated by increasing the expression of GAD-67. Tyrosine hydroxylase is upregulated to enhance dopamine in the striatum [148]. Linalool antagonizes glutamatergic receptors and activates GABA receptors [149]. Linalool regulates serotonin transporters to provide free serotonin available in the synapse area, as shown in Fig. 5 (b) [1].

#### 2.4.2. *Sweet lime*

*Citrus limetta* belongs to the Rutaceae family, which has a good number of polyphenols and is categorized as an antioxidant fruit [150]. Its bioactive ingredients are potent antioxidant, anti-inflammatory, anti-cancer, and neuroprotective [151,152]. Citrus limetta or sweet lime has been usually used to treat peptic ulcers, respiratory problems, digestion, cancer, jaundice, and anxiety [153]. Shah et al. [153] aimed at examining the anxiolytic effects of fruit extracts in Swiss albino mice utilizing an elevated plus maze model and varied doses of 100, 200 and 400 mg/kg of petroleum ether, chloroform, methanol, and water. As a rule, diazepam was used at 2 mg/kg. Findings showed that, when compared to the action of diazepam, methanol extract of fruits 400 mg/kg dose of *Citrus limetta* increased the average time spent in the open arms of the EPM. This study demonstrated that the plant may act as an anti-anxiety agent.

**Table 1**
The anxiolytic effect of different fruits.

| Intervention | Dose and duration | Experimental subjects | Route of exposure | Methodology | Findings | Ref |
|---|---|---|---|---|---|---|
| Banana | 130 g banana for 14 days | Human | Oral | (n = 12)<br>Group 1: Control (new patients)<br>Group 2: Given 2 bananas per day<br>Group 3: Given 3 bananas per day<br>(Old patients)<br>Group 4: Given 2 bananas per day<br>Group 5: Given 3 bananas per day | ↓ HAM-A score ($p < 0.05$) | [49] |
| Blueberry powder | 5 % (w/w) supplementation in RD for 2 weeks | Post-TBI rats (2 weeks later) | Oral | (n = 8)<br>Group 1: RD for rats with sham surgery<br>Group 2: RD for rats with post-TBI<br>Group 3: BB supplemented RD for rats with post-TBI | ↓ 4-HNE ($p = 0.043$)<br>↓ CaMKII ($p = 0.002$)<br>↓ BDNF ($p = 0.012$) | [53] |
| Blueberry concentrate | 30 mL concentrate/100 mL juice for 20 days | Human | Oral | (n = 15)<br>Group 1: Placebo<br>Group 2: Tart cherry<br>Group 3: Blueberry | ↓ BDI ($p = 0.041$)<br>↓ COOP WONKA ($p = 0.019$)<br>↓ STAI trait ($p = 0.023$) | [54] |
| Strawberry | 250 mg/kg extract for 8 weeks | Rats | Oral | (n = 8)<br>Group 1: Water and saline<br>Group 2: Water for 2 weeks<br>Added D-galactose and $AlCl_3$ for 6 weeks (three kinds of strawberry extract)<br>Group 3: Fresh<br>Group 4: Boiled<br>Group 5: Frozen | Normalised the levels of:<br>$Nrf_2$<br>PPAR<br>LDH | [124] |
| Black Currant extract | 200 mg/kg for 14 days | Rats | Oral | (n = 6)<br>Group 1: Control<br>Group 2: Given 1 mg/kg Scopolamine<br>Group 3: Given 120 mg/kg Piracetam (Three types of *Grewia asiatica* extracts were used)<br>Group 4: 18.3 % petroleum ether (PEGA)<br>Group 5: 12.5 % chloroform (CEGA)<br>Group 6: 15.4 % methanol (MEGA) | ↓ EMT ($p = 0.001$)<br>↓ AChE ($p < 0.001$)<br>↓ LPL assay ($p < 0.001$) | [60] |
| Grape pomace | Given 1500 mg/mL juice for 3 days | Rats | Oral | (n = 4)<br>Group 1: Control<br>Group 2: Given 300 mg/kg | AI ($p = 0.047$) | [170] |
| Grapes | 10 g/kg grape powder freeze powder in diet given for 21 weeks | Rats | Oral | (n = 5)<br>Group 1: STD<br>Group 2: HFD<br>Group 3: HF1G | ↓ OFT ($p < 0.60$) | [73] |
| Pomegranate | Given PSE and PJ for three weeks | Rats | Oral | (n = 10)<br>Group 1: Control<br>Group 2: Given 10 mg/kg PQ twice per week for 3 weeks<br>Group 3: Given 500 mg/kg PSE for 2 weeks and add 10 mg/kg PQ in the third week<br>Group 4: Given 40 % sol. of 5 mL PJ for 2 weeks and add 10 mg/kg PQ in the third week | ↑ TH ($p < 0.001$)<br>↑ ATP ($p < 0.05$)<br>PSE:<br>↓ MDA with $p < 0.01$<br>↑ DOPAC and DA ($p < 0.001$)<br>PJ:<br>↓ MDA ($p < 0.05$)<br>↑ DOPAC and DA ($p < 0.05$) | [84] |
| Opuntia | Given 100 mg/kg for 21 days | Rats | Intraperitoneal | (n = 7–10)<br>Group 1: Control<br>Group 2: Given 1 mg/kg Diazepam (sub-extracts based on extraction)<br>Group 3: MeOH, EtOA, n-Hexane, CH2CL2, n-BuOH, $H_2O$ (sub-extracts based on chromatography)<br>Group 4: Fr. A, Fr. B, Fr. C, Fr. D, Fr. E | Sedative effect ($p < 0.001$)<br>Sleeping effect ($p < 0.001$) OFT ($p < 0.01$) | [93] |
| Passion fruit | Given *P. tenuifila* solution for 14 days | Rats | Oral | (n = 6)<br>Group 1: ve control of water<br>Group 2: +ve control with Diazepam and Fluoxetine<br>Group 3: 200 mg/kg fruit extract<br>Group 4: 400 mg/kg fruit extract | Both are anticonvulsant ($p < 0.05$) with 400 mg/kg fruit extract | [100] |
| Piper nigrum extract | Given sol. for 14 days | Rats | Oral | (n = 7)<br>Group 1: Control<br>Group 2: Given 1 mg/kg DZP | ↓ EMT ($p < 0.001$) | [132] |

(*continued on next page*)

**Table 1** (*continued*)

| Intervention | Dose and duration | Experimental subjects | Route of exposure | Methodology | Findings | Ref |
|---|---|---|---|---|---|---|
| | | | | Group 3: Given 400 mg/kg MEPNF<br>Group 4: Given 200 mg/kg MESIS | | |
| Piper nigrum essential oil | Given 0.01 % sol. for 21 days | Rats | Oral | (n = 6)<br>Group 1: Control<br>Group 2: Given 1 mg/kg DZP<br>Group 3: Given 5 mg/kg PNEO<br>Group 4: Given 10 mg/kg PNEO<br>Group 5: Given 50 mg/kg PNEO | ↓ OFT ($p < 0.01$) | [133] |
| Blackberry juice | 8.7 mL/kg for 21 days | Rats | Orogastric | (n = 45)<br>Group 1: Water (variation in dosages based on the level of anthocyanins)<br>Group 2: Low dose (2.6 mg/kg)<br>Group 3: Intermediate dose (5.83 mg/kg)<br>Group 4: High dose (10.57 mg/kg)<br>Group 5: Diazepam (2 mg/kg) | AI showed significant results with Diazepam with a p-value (<0.007) for the intermediate dose (5.83 mg/kg) | [115] |
| Bitter orange | Given 8 drops for 3 days | Human | Aromatherapy | (n = 30)<br>Group 1: Control<br>Group 2: 20 % bitter orange extract | ↓ VAS ($p < 0.001$) | [147] |
| Sweet lemon | Given extract for 21 days | Rats | Oral | (n = 11<br>Group 1: Control<br>Group 2: Given 2 mg/kg Diazepam<br>Group 3: Petroleum ether fruit extract (100, 200 and 400 mg/kg)<br>Group 4: Chloroform fruit extract (100, 200 and 400 mg/kg)<br>Group 5: Methanol fruit extract (100, 200 and 400 mg/kg)<br>Group 6: Aqueous fruit extract (100, 200 and 400 mg/kg) | ↑ EPM compared with diazepam with a p-value <0.05 | [153] |

RD: Regular diet, TBI: Traumatic Brain Injury, AI: Anxiety Index, 4-HNE: 4-Hydroxy Non-Enal, CaMKII: Calmodulin protein kinase 2, BDNF: Brain-Derived Neurotrophic Factor, BDI: Beck Depression Inventory, STAI: State-Trait Anxiety Index, PPAR: Peroxisome Proliferator Receptor, LDH: Lactate Dehydrogenase, HAM: Hamilton, EMT: Elevated Maize Test, AChE: Acetyl Choline Esterase, LPL: Lipoprotein Lipase, MDA: Malondialdehyde, SOD: Superoxide Dismutase, GSH: Glutathione, PSE: Pomegranate Seed Extract, PJ: Pomegranate Juice, OFT: Open Field Test, TH: Tyrosine Hydroxylase, and VAS: Visual Analog Scale.

*2.4.2.1. Anxiolytic mechanism.* D-Limonene, β-Myrcene, and β-Linalool are major constituents responsible for its anxiolytic potential [154]. Myrcene in its extract is accountable for its sedation potential [155,156]. Inhibition of neuronal activity to relieve stress is attributed to the great concentration of myrcene [157]. The involvement of GABAergic neurons is linked with their inhibitory potential. It enhances cholinergic activity while reducing oxidative damage and neuroinflammation. The reduction of prevented inflammation while stimulating the activity of malondialdehyde, gluatathione, superoxide dismutase, and catalase leads to the anti-oxidative mechanism by scavenging free radicals. Acetylcholine is restored by maintaining its functionality that was lost by the increased activity of acetylcholinesterase (AChE). Reducing this enzyme makes this neurotransmitter available for cognition. Some biomarkers which signal damage in the physiology of the brain are also reduced significantly *i.e.,* amyloid-beta peptide and brain-derived neurotrophic factor (BDNF), as shown in Fig. 5 (c) [158].

### 2.5. Other fruits

Some other fruits have been proven to improve mental health yet have not been supported by strong clinical evidence in recent years. They have been shown to have a therapeutic impact on various diseases. Mangoes, grapes, blueberries, pomegranates, apples, hawthorn, and avocados have been widely studied for their polyphenol content. These are associated with protecting endothelial function, managing blood lipids, and blood pressure, and exerting anti-inflammatory effects in combating diseases like Alzheimer's and Parkinson's [159–161]. Among these are dates loaded with thiamine, riboflavin, pyridoxine, folate, calcium, and potassium, which nourish the body and maintain its mental health [162]. Apples are enriched with cyanidin-3-galactoside, a major anthocyanin, antioxidant and anti-inflammatory [163,164]. It also activates brain-derived neurotrophic factors to stabilize neurotransmission [165]. Pears are rich in polyphenols and carotenoids [166], which are associated with a reduction in stress hormones in a systemic way [167]. Kiwi fruits are rich in vitamin C and other antioxidant flavonoids [168]. Papayas are packed with vitamin C and B vitamins and phenolics to exhibit antioxidant potential, which may aid in memory improvement and cognitive behaviours [169]. Other fruits that have a good amount of vitamin C, vitamin $B_6$, vitamin $B_9$, vitamin $B_{12}$, magnesium, potassium, calcium, and phenolics like anthocyanins, even in minor quantities, may have an impact on mental performance. Regular intake of various fruits promises various carotenoids and phenolic compounds and prevents or delays the onset of neurodegeneration.

## 3. Clinical findings

Certain fruits have shown significant improvement in behaviour and physiological processes due to anxiety. Clinical trials have evidenced a remarkable reduction in anxiety through various tools of assessments, *i.e.,* anxiety indexes, behavioral tests (EPM, EMT, Central zone test and OFT), HAM-A, BDI, COOP WONKA, STAI trait, biomarkers or enzymes ($Nrf_2$, PPAR, LDH, AChE, MDA, SOD, GSH, TH, ATP, DOPAC, DA, LPL, 4-HNE, CaMKII, BDNF), an anticonvulsant effect, sedation potential, sleep-inducing effect etc. when significant doses of fruit extracts were given to subjects for a specific time. The following Table 1 is depicted to show the summary of experimental studies conducted to assess the anxiolytic effect of fruits for five years.

## 4. Discussion and conclusion

The ultimate deduction from reviewed data has concluded that food is equally responsible for anxiety besides social and environmental factors. Among them, the anxiolytic effects of fruits are attributed to their bioactive nature and micronutrient profile. Some fruits are discussed in this article with their anxiety-lowering effects. These fruits are rich in phytonutrients that play their part beyond basic nutrition. Anthocyanins are major phytochemicals that show involvement in better functioning of the central nervous system. These are chiefly present in berries and responsible for their effective role in mental health. They can efficiently cross the blood-brain barrier to cure brain disorders. Significant results are seen in intervention studies where stress level was lowered after their intake of an ample amount. Opuntia species have sedation potential and neuromodulatory effects. Black-pepper fruit mediates inhibitory neurotransmitters to relax the nervous system. Citrus species preserve hormonal regulation and neurotransmission. Other fruits having vitamin B complex and antioxidant capacity play a vital role in signaling pathways. Findings suggest that fruits can act as a preventive as well as a therapeutic approach to tackle cognitive impairments and behavioral abnormalities. These nutrients directly or indirectly regulate neural and psychological activities along with physiological processes. Findings suggest that fruits can act as a preventive as well as a therapeutic approach to tackle cognitive impairments. However, this clinical evidence doesn't demonstrate the actual mechanism of neural pathways. Further studies are needed to implement the described strategies for the treatment of anxiety.

## CRediT authorship contribution statement

**Sana Manzoor:** Writing – original draft, Data curation, Conceptualization. **Allah Rakha:** Writing – review & editing, Conceptualization. **Ammar B. Altemimi:** Writing, review and editing. **Tayyaba Tariq:** Writing – review & editing. **Seemal Munir:** Writing – review & editing. **Farwa Tariq:** Writing – review & editing, Visualization. **Aysha Sameen:** Writing – review & editing, Supervision, Conceptualization. **Gholamreza Abdi:** Writing – review & editing, Supervision, Conceptualization. **Rana Muhammad Aadil:** Writing – review & editing, Supervision, Data curation, Conceptualization.

## Declaration of competing interest

None.

## Data availability

Data will be made available on request.

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