Pol. J. Environ. Stud. Vol. 33, No. 4 (2024), 4031-4042
DOI: *10.15244/pjoes/177428* ONLINE PUBLICATION DATE: 2024-04-25

Original Research

Neuropharmacological Evaluation and Antioxidant Potential of *Aloe Barbadensis*, *Capparis Spinosa* and *Senegalia Senegal* Extract in Mice

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Received: 5 November 2023
Accepted: 21 December 2023

Abstract

Aloe barbadensis, *Capparis spinosa*, and *Senegalia senegal* are popular in traditional medicine due to their therapeutic effects. We aimed to assess the neuropharmacological potential of their extracts, including the impact on pain-relief, anxiety, depression, muscle relaxation, and motor coordination. BALB/c mice were administered with standardized doses of *A. barbadensis*, *C. spinosa*, and *S. senegal* extracts, and their behavior was recorded through various neurobehavioral tests. The antioxidant potential of the extracts was also evaluated by DPPH assay. A differential response was observed among the three extracts for analgesic activity. *A. barbadensis* showed an increase in latency time after an increase in dose, while *C. spinosa* and *S. senegal* exhibited a biphasic response. *A. barbadensis* showed very good anxiolytic effects and best anti-depression effects. *S. senegal* exhibited the best antioxidant activity, followed by *A. barbadensis* and *C. spinosa*. This shows that these plants could counteract oxidative stress and protect neurons from potential damage caused by free radicals. The observed anxiolytic, muscle relaxant effects, and enhanced antioxidant potential of the selected plants in BALB/c mice, indicate their potential therapeutic value in neuroprotective strategies and the treatment of oxidative stress-related neurological disorders. However, further investigations into their underlying mechanisms and long-term safety profiles are suggested before considering their translation into clinical applications.

Keywords: *Aloe barbadensis*, *Capparis spinosa*, *Senegalia senegal,* neuropharmacology, natural products, antioxidant, plant extract

Introduction

Plant extract-based neuropharmacological research holds promise in identifying new treatments or supportive therapies for neurological disorders, cognitive enhancement, anxiety, oxidative stress related ailments and pain relief [1, 2]. Exploring plant based extract for therapeutic purpose is a fascinating and important area of scientific research that has garnered significant attention throughout history. Their usage in the traditional medicine such as Ayurveda, and Traditional Chinese Medicine has been in practice

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for centuries for treating various ailments [3]. Hence, exploring plants of medicinal value can lead to the discovery of novel therapeutic uses and inspire modern drug development [4]. Since the natural products often interact with multiple targets within biological systems, they offer the potential for multi-target therapeutics [5]. This can be particularly beneficial for complex diseases like neurological disorders, with multiple underlying factors. Additionally, plants have been explored for their potential analgesic properties and have been used for centuries in traditional medicine to alleviate pain [6, 7]. They contain various bioactive compounds that can interact with the nervous system and influence pain perception. An example is the use of Willow (*Salix* spp.) bark for headache and musculoskeletal pain relief. It contains salicin, which is similar in structure to aspirin, a well-known analgesic and anti-inflammatory medication [8]. Another example is Cannabis (*Cannabis sativa*), rich in cannabinoids like tetrahydrocannabinol and cannabidiol, which have been the subject of extensive research for their potential analgesic effects [9, 10]. Medical cannabis is now being utilized for chronic pain management, particularly in cases of neuropathic pain and pain related to cancer.

Plants have also been studied for treatment of anxiety and shown promising results in experiments. *Passiflora incarnata* Linn. has been used to treat insomnia in traditional medicine [11, 12]. It has shown anti-anxiety effects in mice models. Hydroalcoholic extract of the *Brassica oleracea* L., comprising alkaloids, phenols, flavonoids and tannins has shown a dose dependent increase in the anti-anxiolytic effects in mice, which were comparable to diazepam [13]. *Humulus lupulus* dry extract (intake of 0.2 g) for a month has shown decreased depression in human clinical trials [14]. Apart from this, plants have also been a therapeutic source for the oxidative stress related diseases including cardiovascular diseases, neurodegenerative disorders, diabetes, and aging-related ailments [15, 16]. Oxidative stress occurs when there is an imbalance between the production of reactive oxygen species (ROS) or free radicals and the body's ability to neutralize them with antioxidants. Excessive ROS can damage cellular components, including proteins, lipids, and DNA, leading to oxidative stress-related conditions [17]. Plant extracts or their derived compounds may scavenge free radicals and protect cells from oxidative damage, offering a preventive or therapeutic approach to combat the oxidative stress-related diseases. Marmitt et al. has reported in a meta-analysis that *Allium sativum* and *Curcuma longa* occupy the top position in clinical research for oxidative stress alleviation. *Ginkgo Biloba* extract, with antioxidant properties, has shown encouraging results against dementia. A dose of 240 mg/day has been reported to improve cognitive function and clinical trials are being conducted for testing its efficacy [18]. Ginger upsurges antioxidants via Nuclear factor kappa-light-chain-enhancer of activated B cells (NFκB) activation, and interaction with Kelch-like ECH-associated protein 1 (KEAP1), in diabetic nephropathy. *Camellia sinensis* L. contains strong antioxidative flavonoids and alleviated albuminuria in a clinical trial on diabetic patients receiving renin-angiotensin inhibition drugs [19].

Aloe barbadensis, Capparis spinosa, and *Senegalia senegal* have captured the interest of researchers due to their medicinal properties. *A. barbadensis* is commonly known as Aloe vera and is a succulent plant renowned for its medicinal properties [20]. Several studies have reported an array of bioactive compounds that contribute to its diverse therapeutic effects [21, 22]. *C. spinosa,* commonly known as caper, is a perennial plant widely distributed in the Mediterranean region and parts of Asia [23]. It has a long history of use in traditional medicine for various health conditions [24]. *S. senegal*, also known as *Acacia senegal*, is a tree native to regions in Africa and the Indian subcontinent [25]. Traditionally, it has been used for its medicinal properties, and modern research has shed light on its potential health benefits based on compound composition. We hypothesized that the extracts of all these plants may have neuroprotective effects, alleviate oxidative damage, and improve overall cellular health, offering hope for more effective treatments and preventive strategies to improve global public health outcomes. Hence, we tested their impact on Bagg Albino (BALB/c) mice as they are a widely used and well-characterized strain with stable and consistent behavioral and physiological characteristics. This makes them suitable for assessing the effects of the plant extracts on locomotor activity, anxiety-like behaviors, and motor coordination. Using this controlled experimental approach helps gather valuable data for translational studies and draw meaningful conclusions to support the hypothesis.

Material and Methods

Plant Material and Chemicals

The identified plant material for *A. barbadensis, C. spinosa,* and *S. senegal* was kindly provided by Prof. Abdulrahman Alsoqeer from plant production and protection department of the Qassim University, KSA. Analytical grade chemicals were purchased from Sigma Aldrich (Fluoxetine; diazepam; diclofenac sodium; Trolox), Merck (L-ascorbic acid/vitamin C; 2,2-Diphenyl-1-picrylhydrazyl; methanol; Folin-Ciocalteu phenol reagent; ferric chloride; HCl) and Riedel-de Haen (Sodium carbonate; Dimethyl sulfoxide). Plant extract was prepared in ethanol and redissolved in methanol, according to the previously described protocol [26].

Hotplate Analysis

This study aimed to evaluate the analgesic activity of the plant extract using the hot plate test. BALB/c mice of

both sexes (n = 6), weighing 18-22 g, were acclimatized to laboratory conditions one hour before the experiment with ad libitum access to food and water. During pre-testing on a hot plate set at 55±0.1ºC, animals with a latency time greater than 15 seconds were excluded [27]. The mice were divided into eight groups, each consisting of six animals. Group I received a saline solution (10 ml/kg), Group II received TramadolR (50 mg/kg intraperitoneally), and Groups III, IV, and V received 100, 200, and 300 mg/kg of the plant extract, respectively (intraperitoneally). After 30 minutes of treatment, the mice were placed on the hot plate, and the latency time (duration without licking, flicking of hind limbs, or jumping) was measured in seconds. A cutoff time of 30 seconds was imposed to prevent tissue damage [28].

To investigate the opioid mechanism in the analgesic activity of the plant extract, Groups VI and VII were treated with naloxone (0.5 mg/kg subcutaneously) followed by plant extract (200 and 300 mg/kg, i.p.) after 10 minutes. Group VIII received TramadolR (30 mg/kg i.p.) after 10 minutes of naloxone injection. The latency time was recorded for all groups at 0, 30, 60, 90, and 120 minutes. Percent analgesia was calculated using the formula: % Analgesia = (Test latency – control latency)/ (Cut-off time – control latency) × 100 [29, 30].

Acetic Acid Induced Wreathing Analysis

This study also aimed to assess the pain-relieving potential of the plant extract. BALB/c mice of both sexes (n = 6) weighing 18-22 g were used for the experiment. The animals were deprived of food for 2 hours before the start of the experiment [31] and were then divided into five groups. Group I received a control injection of normal saline (10 ml/kg), Group II was administered the standard drug diclofenac sodium (10 mg/kg) [32], and the remaining Groups III, IV, and V were injected intraperitoneally with 100, 200, and 300 mg/kg of the plant extract, respectively. After 30 minutes of saline, diclofenac sodium, or plant extract injection, the mice were treated with 1% acetic acid intraperitoneally. The number of abdominal constrictions (writhes) was counted for 10 minutes, starting 5 minutes after the acetic acid injection [33].

Staircase Test

The anxiolytic effect of the plant extract was evaluated using the staircase test with slight modifications to the standard protocol. A staircase apparatus consisting of five identical steps with dimensions 2.5 x 9 x 10 x 9 x 7.5 cm was placed on an elevated surface [34]. The experimental mice were divided into control, standard, and treated groups, each comprising six mice. The control group received a treatment of distilled water (10 ml/kg), the standard group was treated with diazepam (1 mg/kg) [35], and the remaining groups were treated with plant extract at doses of 0.3, 0.4, and 0.5 g/kg of body weight. After 30 minutes of treatment, each mouse was placed on the first step of the elevated staircase, and their behavior was observed for 3 minutes. The number of steps climbed and the number of rearings were recorded for each animal. A step was considered as climbed only if the mouse had placed all four paws on the step [28]. To maintain hygiene and cleanliness, the staircase was cleaned from feces and urine after each mouse performance.

Traction Test

The neuromuscular function was assessed using the traction test. A metal wire coated with rubber was utilized for this procedure, with both ends rigidly supported by stands positioned approximately 60 cm above the laboratory bench [36]. Different groups, each comprising six animals, were administered different treatments: diazepam (1 mg/kg), distilled water (10 ml/kg), and varying doses of plant extracts (0.3, 0.4, and 0.5 g/kg). After 30, 60, and 90 minutes of treatment, the animals underwent the traction test. Each animal was hung by their hind legs from the wire, and the duration of hanging was recorded for 5 seconds [36]. Failure to hang for less than 5 seconds was indicative of the presence of muscle relaxant activity, while the ability to hang for the full 5 seconds indicated otherwise.

Forced Swimming Test

The antidepressant activity of the extract was assessed using the forced swimming test (FST) [37]. Prior to the experiment, all mice were trained for swimming in a bath with dimensions of 42 x 19 x 19 cm. The bath was filled with water at a temperature of 25±2ºC up to a depth of 15 cm [38]. The acclimatized experimental mice were divided into five groups, each comprising six animals. The control group received no treatment, the standard group was administered fluoxetine (an established antidepressant drug), and the remaining groups were treated with different doses of the plant extract (0.3, 0.4, and 0.5 g/kg). Following the respective treatments, the mice were allowed to swim in the bath for a duration of 6 minutes [39]. The duration of immobility during the last 240 seconds of the swimming period was recorded for each animal.

Effect of the Inclined Plane

The inclined plane test is a neuropharmacological experiment employed to evaluate muscle relaxant properties and motor coordination in laboratory animals [40]. The test apparatus comprises two plywood boards, with one serving as the base and the other fixed at an angle of 65 degrees to the base. The experimental mice were divided into different groups (n = 6), each receiving specific treatments: diazepam (1 mg/kg), distilled water (10 ml/kg), and varying doses of plant extracts (0.3, 0.4, and 0.5 g/kg). After 30, 60, and 90 minutes of treatment,

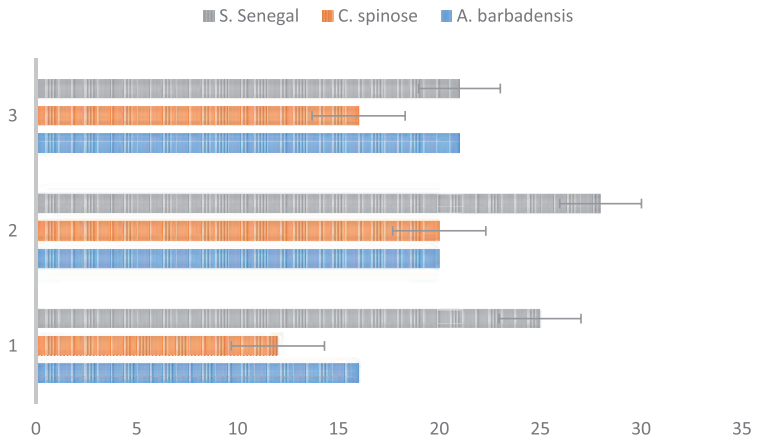

Fig. 1. Wreathing analysis results of studied plant extracts.

the animals were placed on the upper part of the inclined plane for 30 seconds to observe their ability to either hang onto the plane or fall from it [41].

DPPH Assay

The 2,2-diphenyl-1-picrylhydrazyl (DPPH) radical scavenging assay was conducted to determine the antioxidant activity of the samples, following a standard protocol as previously described [42]. Vitamin C was used as the positive control. The assay measures the hydrogen atom or electron donation abilities of the samples and standards by monitoring the bleaching of the purple-colored methanol solution of DPPH radicals [43]. The experiments were performed in triplicate. Initially, 1 mM solution of DPPH radical in methanol was prepared, and 1 ml of this solution was mixed with 3 ml of the sample solutions (extracts/fractions) in methanol, each containing concentrations ranging from 10 to 100 ug for various fractions and from 5 to 100 ug for pure compounds. A control solution without any sample was also prepared. The mixture was allowed to stand in the dark for 30 minutes, and the absorbance was then measured at 517 nm. A decrease in the absorbance of the DPPH solution indicates an increase in the DPPH radical scavenging activity of the samples. The scavenging of free radicals by DPPH was calculated as the percent radical scavenging activity (RSA) using the following formula:

$$\% \text{ DPPH} = (\text{OD control} - \text{OD sample}) \times 100 / \text{OD control [44]}$$

Results and Discussion

Analgesic Activity

Hotplate and acetic acid induced wreathing analysis test indicated a differential response for analgesic activity among the three extracts. The latency time increased after increase in dose for *A. barbadensis*, but decreased for *C. spinosa* and *S. senegal* after increasing on half hour time elapsed, and later decreasing again (Table 1). The effect was not dose dependent for *C. spinosa* and *S. senegal*, indicating a possible biphasic response. Such biphasic responses have been reported in certain natural products [45, 46], suggesting the presence of multiple bioactive compounds with opposing effects or interactions between different components. Further investigations are required to identify the specific compounds responsible for this response and elucidate their mechanisms of action. The lack of a clear dose-response relationship for *C. spinosa* and *S. senegal* indicates that their analgesic effects might not be solely dependent on the administered dose and complex pharmacological interactions may be involved, or the analgesic pathways may be blocked at higher doses. Understanding this in depth can have implications for dosage recommendations and therapeutic applications. For acetic acid writhing test, *C. spinosa* demonstrated best anti-pain results, followed by *A. barbadensis* and *S. senegal* (Fig. 1).

Literature suggests that *A. barbadensis* contains compounds like aloin and aloesin [47]. These compounds possess anti-inflammatory and analgesic properties [48], possibly through the inhibition of prostaglandin [49]. *C. spinosa* has been reported to contain flavonoids and phenolic compounds [50]. These are responsible for potential analgesic effects through the modulation of neurotransmitters and ion channels [51]. Assane et al. have reported the presence of alkaloids, flavonoids, tannins and saponins in *S. Senegal* [52]. These classes of compounds are also known to have analgesic and anti-inflammatory properties [53]. Hence, the pain relief activity of this plant may be attributed to the presence of these compounds. Previously, Taki et al. have also reviewed the analgesic properties of *S. senegal* [54].

Table 1. Hot plate analysis of studied plant extracts, showing latency time.

Test Compound	Animals	0 mints/sec	30 mints/sec	60 mints/sec	90 mints/sec	120 mints/sec
A. barbadensis	1	9.2	14.1	15.2	16.4	19.2
	2	8.6	13.7	16.6	16.3	19.6
	3	8.1	13.3	15.3	16.9	17.3
C. spinose	1	8.2	12.1	9.6	8.9	7.3
	2	8.7	12.4	10.3	9.1	8.3
	3	9.5	12.7	11.2	9.3	8.1
S. senegal	1	7.2	11.5	7.6	6.1	5.4
	2	8.4	11.8	8.8	7.4	7.9
	3	7.9	12.7	10.4	8.1	7.2

Anti-anxiety Potential Determination

The staircase test is a behavioral test used to assess the anxiolytic properties of substances. *A. barbadensis* showed very good potential of anxiety reduction, with no movement up and down the stairs at all (Table 2). This was followed by *S. senegal,* while *C. spinosa* showed decreased anxiety at around 60 minutes and later lost effect. The observed anxiolytic effects of the plant extracts in the staircase test could be attributed to their interactions with neurotransmitter systems implicated in anxiety regulation. This may be due to modulation of neurotransmitters and blocking receptors responsible for releasing hormones that cause stress or anxiety. Previously, natural substances have been reported to reduce anxiety [55, 56]. Bawish et al. have reported reduced anxiety-like behavior in Wistar rats with Aloe vera gel powder, due to its high polyphenol content [57]. Hence, *A. barbadensis* seems a promising candidate for further exploration as an anxiolytic agent. Low doses of *S. senegal* have been reported previously to have potential anxiolytic activity, while it has demonstrated antidepressant and tranquillizing behavior at higher doses [58]. *C. spinosa* is known to possess muscle relaxing, tranquillizing and anticonvulsant behavior [59]. However, it showed transitory anxiolytic effect, indicating lower potency in comparison. Further research is needed to elucidate the specific mechanism and whether the activity would be sustained at higher doses or not. Our findings align with the existing literature on the anxiolytic potential of Aloe vera and suggest *A. barbadensis* as a promising candidate for further exploration as an anxiolytic agent.

Traction and Inclined Plane Analysis

Traction analysis was done to assess the muscular strength and neuromuscular function after extract administration. The force generated by the mice's hind limbs against the wire was measured. The force decreased with time for *A. barbadensis*, increased at 60 minutes for *C. spinosa* and then decreased again,

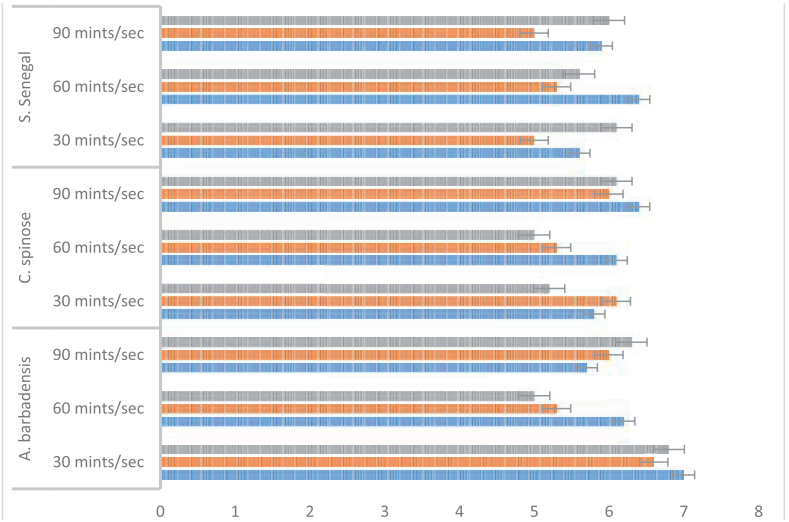

Fig. 2. Traction analysis of studied plant extracts, showing latency time.

Table 2. Staircase test analysis of studied plant extracts.

Test Comp	Replicate	30 mints /no of rearing	30 mints/ Stairs up and down	60 mints /no of rearing	60 mints/ Stairs up and down	90 mints /no of rearing	90 mints/ Stairs up and down
A. barbadensis	1	2	0	0	0	0	0
	2	2	0	0	0	0	0
	3	3	0	0	0	0	0
C. spinose	1	7	7	3	0	3	8
	2	9	6	0	2	2	5
	3	6	5	1	1	4	6
S. senegal	1	2	0	0	0	0	0
	2	2	1	2	0	1	0
	3	3	2	1	0	2	0

while it did not show consistent a pattern for *S. senegal* (Fig. 2). The temporal aspect of plant extract action highlights the importance of considering the appropriate timing for therapeutic applications and may offer insights into the optimal dosing regimens.

All plant extracts showed hanging time greater than 30 sec for inclined plane analysis, compared to the control. The increase in hanging time observed in all plant extract-treated mice compared to the control suggests an improvement in muscle endurance and neuromuscular coordination. This finding aligns with previous literature suggesting potential adaptogenic properties of these natural substances [60-62], supporting their traditional use in promoting physical performance and vitality. Understanding the impact of these plant extracts on muscular strength and neuromuscular function has implications beyond potential therapeutic applications and strengthening muscles of elderly to avoid falls [63]. Athletes and individuals seeking to enhance exercise performance may find these natural substances valuable in supporting muscle endurance and coordination during physical activities.

FST for Anti-Depression Effect

A. barbadensis showed the best anti-depression effect, with reduced struggle to escape from the water (Fig. 3). To further establish the antidepressant potential of studied plants, identifying the specific bioactive compounds responsible for the observed effect is crucial. Targeted isolation and characterization of these compounds can aid in developing standardized extracts or new pharmacological agents for depression management. While the anti-depression effect of *A. barbadensis* is promising, it is essential to consider its safety profile and potential side effects. Aloe vera has been generally regarded as safe when used topically or in moderate amounts for oral consumption, but reports of its gel hypersensitivity and contact dermatitis exist [64]. Boudreau and Beland have also listed erythema, kidney dysfunction, diarrhea, and drug interactions associated with its ingestion [65]. Therefore, a comprehensive safety evaluation is necessary before considering its use as an antidepressant.

Antioxidant Potential

Best anti-oxidant potential was shown by *S. senegal*, indicating its ability to effectively scavenge free radicals and mitigate oxidative stress. This was followed by *A. barbadensis* and then *C. spinosa* (Fig. 4). *Acacia senegal* has been previously reported to inhibit the HMG-CoA reductase, leading to increase in antioxidants in rabbits and *in vitro* studies [66]. Lopez et al. have also reported antioxidant potential of Aloe vera leaf skin extract due to phenols (gentisic acid, epicatechin and quercitrin) [67]. Lee et al. have reported isolation of 8-C-β-d- [2-O-(E)-coumaroyl]glucopyranosyl-2-[2-hydroxy]propyl-7-methoxy-5-methylchromone, an anti-oxidant compound from *A. barbadensis* Mill, using thin layer chromatography [68]. Aliyazicioglu et al. have reported 16 phenolic constituents in the *C. spinosa* [69], while Yang et al. reported a new anti-oxidant cappariside (4-hydroxy-5-methylfuran-3-carboxylic acid, in the fruits of *C. spinosa* in addition to known compounds [70].

The varying antioxidant potentials of *S. senegal*, *A. barbadensis*, and *C. spinosa* may be attributed to their distinct phytochemical compositions. Further analysis of the specific phytochemicals in each extract can help identify the major contributors to their antioxidant activity. The findings will have implications for potential therapeutic applications in oxidative stress-related conditions. Oxidative stress is involved in various diseases, including neurodegenerative disorders, cardiovascular diseases, and diabetes [71]. Harnessing the antioxidant properties of these natural extracts could offer a complementary approach to managing these conditions.

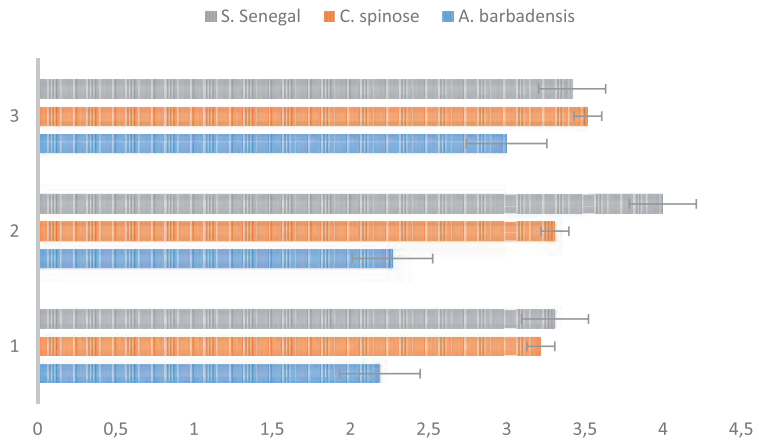

Fig. 3. FST analysis results of studied plant extracts, showing latency time.

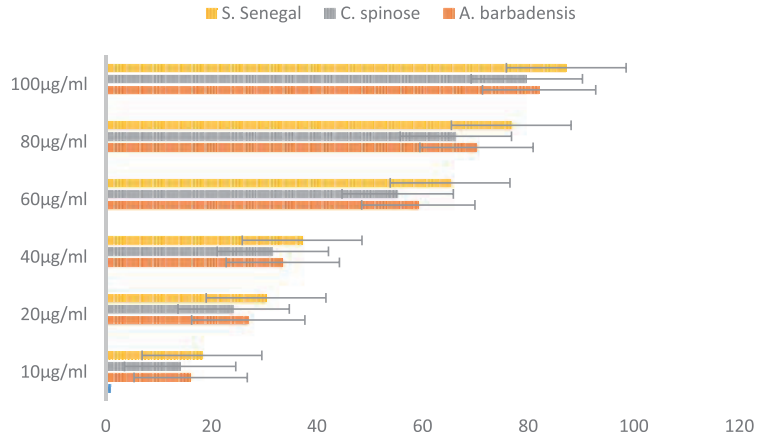

Fig. 4. Antioxidant potential results of studied plant extracts at various concentrations.

Discussion

Utilizing plant-derived compounds aligns with the trend towards natural and holistic approaches in healthcare, appealing to individuals seeking alternatives to synthetic drugs [72]. One of the significant advantages of using plant extracts is their natural sourcing and easy availability [73]. Plant compounds are recognized for their diverse pharmacological properties [74], encompassing anti-inflammatory and analgesic effects [75], anti-anxiety and anti-depression attributes [76], augmentation of muscular strength [77], enhancement of neuromuscular function, and antioxidant capabilities [78]. Turmeric, containing the active compound curcumin, stands out for its potent anti-inflammatory and analgesic properties, alongside robust antioxidant effects [79]. Chamomile and Lavender is renowned for its calming effects, potentially contributing to anti-anxiety and anti-depressant outcomes [80, 81]. Ginger, with its anti-inflammatory and analgesic effects, is employed to alleviate pain and inflammation, while also demonstrating antioxidant properties [82]. These properties have also been studied in mouse models using *Thymus vulgaris* extract [26].

A.barbadensis, *C. spinosa*, and *S. senegal* are all well-known medicinal plants with a history of traditional usage. However, their utility in anti-inflammation, anti-depression, muscular strength etc., was not demonstrated in pre-clinical models. The selected plant extracts were studied for this purpose and demonstrated neuropharmacological effects without severe adverse reactions in the BALB/c mice. This suggests that these extracts might have lower side effect profiles compared to some conventional treatments for neurological disorders. This aspect is particularly important, as minimizing adverse effects of a drug is crucial for enhancing patient compliance and overall well-being [83, 84]. The compound Aloin from the genus Aloe has previously demonstrated antioxidant effects and anti-inflammatory properties through phosphorylation of proteins in NF-κB and JAK/STAT pathway [85]. Yagi et al. have also demonstrated these properties for aleosin from *A. barbadensis* [86]. Another compound Aloe-emodin that exists in *A. barbadensis* has been implicated in neuroprotective properties [87]. Other compounds and their role in neuropharmacology needs to be studied. Yang et al. have reported cappariside from *C. spinosa* as an antioxidant [70] while Zhou et

al. [88] demonstrated anti-inflammatory properties of ginkgetin from this plant. Other compounds linked with neuroprotection as well as their allied pathways remain yet to be elucidated. As for the *S. senegal*, LOTUS database (https://lotus.naturalproducts.net/search/simple/Senegalia%20senegal; retrieved 14 November 2023) shows presence of 2-octadecenoic acid and Trans-2-octadecenoic acid in this plant. However, no relation with neuroprotective, antioxidant or muscular strength of these compounds has been reported in literature. Other compounds may also be isolated and tested for these properties from this plant.

The observed differential responses among the extracts for various neurobehavioral and antioxidant parameters highlight the potential for synergistic effects. Combining these extracts in specific ratios might result in enhanced therapeutic outcomes, providing a multifaceted approach to addressing the complex pathophysiology of oxidative stress-related neurological disorders. Such synergies could involve targeting multiple pathways, including neurotransmitter modulation, antioxidant defense, and anti-inflammatory activities. Our findings also hold promising implications for the management of neurological disorders characterized by oxidative stress, such as Alzheimer's disease and Parkinson's disease [89]. Free radicals and oxidative stress play a significant role in the progression of these disease conditions [90]. Studied plant extracts, with their potent antioxidant potential, could counteract oxidative damage, thereby potentially slowing down disease progression and protecting neurons from further harm. The anxiolytic and anti-depression effects of the studied plants are highly relevant to neurological disorders, as anxiety and depression often coexist with conditions like Alzheimer's disease and Parkinson's disease [91]. The natural anxiolytic properties of *Aloe barbadensis* could offer relief to patients struggling with emotional distress alongside their neurological symptoms. Given the anxiolytic, muscle relaxant effects, and enhanced antioxidant potential of these plant extracts, they hold promise as components of neuroprotective strategies. These strategies could involve combining these extracts with other neuroprotective agents, lifestyle modifications, and cognitive interventions. By addressing multiple aspects of the disorders, these extracts could contribute to a comprehensive approach to disease management.

The observed effects of these plant extracts on muscular strength and neuromuscular function open avenues for potential benefits in physical performance and exercise endurance. While the initial assays have provided promising results, it is imperative to delve deeper into the identification of specific bioactive compounds responsible for these effects. Previously, polyphenols such as resveratrol & curcumin, terpenoids like ursolic acid, tanshinone IIA, & celastrol, as well as flavonoids, alkaloids such as tomatidine & magnoflorine, as well as vitamin D, have demonstrated substantial efficacy against skeletal muscle atrophy by regulating musculature and facilitating locomotion [92]. The identification of specific compounds from the studied plants through GCMS or relevant techniques could be explored in this direction.

Nevertheless, there were some limitations of this study as well, as we used a specific dose range for the extracts and this might not represent the full spectrum of potential effects. The BALB/c mouse model also cannot fully recapitulate the cellular conditions found in the human body [93]. Thus, translational challenges may exist when extrapolating findings from mice to humans, due to the differences in metabolism, pharmacokinetics, and physiological responses [94]. The study also did not extensively explore the underlying molecular mechanisms responsible for the observed effects and we propose that further research in this direction could enhance the credibility and applicability of our findings. Hence, it is proposed that the impact on serotonin, dopamine production and intracellular signaling pathways should be attempted in light of the obtained findings.

Future work could also focus on enzyme-linked immunosorbent assay (ELISA) and imaging techniques to quantify neurotransmitters and proteins in specific brain regions, real-time observation of blood flow changes and neuroreceptor binding. Other electrophysiological techniques, like electroencephalography (EEG) and patch clamp recordings, provide a means to examine overall brain function and individual neuron activity under the impact of plant extracts for anti-anxiety or depression could also be conducted. Polymerase chain reaction (PCR) and western blotting to detect gene expression and protein levels associated with neuropharmacological effects could also enhance the findings at molecular level., histological techniques Integrating approaches like *in vitro* models (utilizing cell cultures could) also offer a comprehensive exploration of the neuropharmacological effects of plant extracts, encompassing behavioral, molecular, and structural aspects of the nervous system.

Conclusion

The comprehensive evaluation of *A. barbadensis*, *C. spinosa*, and *S. senegal* extracts through various assays has provided valuable insights into their diverse biological activities. *A. barbadensis* demonstrated significant analgesic, anxiolytic, and anti-depression effects, making it a multi-faceted candidate for potential therapeutic applications. *C. spinosa* exhibited robust anti-pain properties and transient anxiolytic effects, suggesting its potential as a targeted analgesic agent. *S. senegal* displayed outstanding antioxidant potential and promising anti-pain and anti-depression effects, highlighting its diverse pharmacological properties. These findings underscore the significance of natural products in the search for novel therapeutic agents for pain management, mood modulation,

and antioxidant defense. Additionally, effects of studied plants on muscular strength and neuromuscular function offer potential benefits for physical performance and exercise endurance. While these natural extracts have shown promising results in the assays conducted, further studies are necessary to elucidate the specific bioactive compounds responsible for their effects and to address safety considerations. Additionally, investigations into their pharmacokinetic profiles and potential interactions with other medications will be crucial for their translation into clinical applications.

Glossary/List of Abbreviations

DPPH: 2,2-diphenyl-1-picrylhydrazyl
RSA: radical scavenging activity
OD: optical density
BALB/c: Bagg Albino strain c mice
ELISA: enzyme-linked immunosorbent assay
EEG: electroencephalography
PCR: Polymerase chain reaction

Author Contributions

SMA conceived and designed the experiments, performed experiments and wrote the paper.

Ethical Consent

The ethical consent for these experiments were obtained from the University Committee on Ethics. The present study was performed according to international, national and institutional rules considering animal experiments.

Conflict of Interest

The author declares no conflict of interest.

Data Availability

All data is within manuscript unless otherwise stated.

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