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Original article

Deciphering the CNS anti-depressant, antioxidant and cytotoxic profiling of methanol and aqueous extracts of *Trametes versicolor* and molecular interactions of its phenolic compounds

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ABSTRACT

The present study sought to evaluate the central nervous system (CNS) depressant, antioxidant, and cytotoxicity activity of methanol and aqueous extract of *Trametes versicolor* (METV and AETV). The CNS activity was assessed by the open field, hole-cross, forced swimming, thiopental sodium-induced sleeping time, hole-board, and rotarod tests in Swiss albino mice. For both extracts, a substantial decrease in locomotion was observed in open field and hole-cross tests. In addition, the molecular docking study has been implemented through Maestro V11.1. The higher dose of METV (400 mg/kg) and the lower dose of AETV (200 mg/kg) exhibited a significant decrease in immobility time in forced swimming test and increased prolongation of sleep in thiopental sodium-induced sleeping time test, respectively. In contrast, a moderate finding was observed for the hole-board and rotarod tests. Additionally, a significant DPPH scavenging assay and a high toxicity effect in brine shrimp lethality assay were observed. Besides, five phenolic compounds, namely baicalin, quercetin, catechin, p-hydroxybenzoic acid, and quinic acid, were used for the molecular docking study, whereas catechin demonstrated the highest binding affinity towards the targets. The findings conclude that the *T. versicolor* could be an alternative source for CNS anti-depressant and antioxidant activity.

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1. Introduction

Depression, which leading cause remains unresolved, is a common mental or psychiatric ailment. Studies have suggested that the imbalance of immunity and enhancements in proinflammatory cytokines might associate with depression (Rana, Behl et al. 2021). Another study based on the monoaminergic system does not proclaim a full perception of depression (Sultana, Mannan et al. 2018). Oxidative stress is related to the development of depression, which is the most accepted hypothesis for depression (Michel, Frangou

et al., 2007). The reports of the World Health Organization (WHO), 121 million people were suffered from clinical depression, the second largest in the world after heart disease (Cryan and Lucki, 2000; Smith, Sketris et al., 2008). Both secondary metabolites and the active drug compounds are prominently derived from medicinal plants. It features prominently in the discovery of new drug molecules, which possibly will be an alternative source of depression treatment (Zhang, Wu et al., 2015; Uddin Mazumdar, Islam et al., 2017). Antioxidants protect the physiological system of our body by protecting the cell against reactive oxygen species (ROS), whereas it also protects the cell from oxidative stress (OS) (Uddin Mazumdar, Islam et al. 2017). OS is caused due to the production of free radicals resulting in cell and DNA damage and various disorders (Festa et al., 2001; Uddin Mazumdar, Islam et al., 2017). OS causes changes in genes' expressions and induces abnormal proteins, which lead to several human disorders, including the development of atherosclerosis, heart disease, and central nervous system (CNS) diseases, cancer, and acquired immunodeficiency syndrome (AIDS) (Hela and Abdullah, 2010; Khatun et al., 2016). The human body's physiology can neutralize the OS by its antioxidant mechanism. But somehow it

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may fail because of the free radicals overproduction. Free radicals are neutralized by antioxidants, whereas plants and vegetables are a natural source of antioxidants. As a result, people are more efficient against OS-related health problems (Nahar et al., 2012; Rahman et al., 2015).

Nature is the best reliable source for potential drugs molecule. The wide range of structural molecules derived naturally leads to new medicines to attain better pharmacologic activity with the least side effects (Muhammad et al. 2015). In contrast, the mushroom has significant nutritional values (fibre, proteins, and vitamins) along with rich antioxidant-property phytochemicals (Puia et al., 2018). There is a substantial need for the development of potential drug molecules for new antioxidants, cytotoxic, and CNS depressants from natural resources. *Trametes versicolor* (L.) is one of the plants of the Polyporaceae family, which is also acknowledged as Turkey tail. Though it is not edible, it is useful in folk medicine for its various pharmacological effects. *T. versicolor* has been reported to have antioxidant (Kamiyama et al., 2013; Puia et al., 2018), anticancer (Cfr Ferreira et al., 2010; Puia et al., 2018), anti-microbial (Puia et al., 2018; ÖzgÖR.et.all., 2016), anti-inflammatory (Kamiyama et al. 2013), immune system boosters (Li et al. 2011) and antidiabetic effects (Puia et al., 2018; Shokrzhadeh et al., 2017). In terms of bioactive compounds, it has been identified polysaccharides, 18-type of amino acids, and 28 phenolic compounds (Puia et al., 2018). However, there are no studies that scrutinized the CNS depressant activity of *T. versicolor*.

Thus, in the present study, methanol and aqueous extracts of *T. versicolor* have been used to assess the antioxidant, cytotoxic, and CNS activities. The study of CNS activity was performed on Swiss albino mice. Additionally, the molecular docking study was performed on phenolic compounds of *T. versicolor* against four different receptors.

2. Materials and methods

2.1. Chemicals and reagents

1, 1-diphenyl, 2-picryl hydrazyl (DPPH) and ascorbic acid was brought from Sigma Chemical Co., USA. And SD Fine Chem. Ltd., Biosar, India, respectively. Imipramine (Square Pharmaceuticals Limited, Dhaka) and diazepam (Square Pharmaceuticals Limited, Dhaka) and vincristine sulfate (Beacon Pharmaceuticals Limited, Dhaka) were procured from the Bangladeshi pharmaceutical company. The Department of Pharmacy, University of Chittagong, Chittagong, Bangladesh have supplied additional analytical-grade chemicals.

2.2. Mushroom collection and extraction

T. versicolor collected from the areas of the University of Chittagong campus. Mr. Sajib Rudra, Taxonomist, Department of Botany, University of Chittagong identified the mushrooms under the accession number of CTGUH SR 2798. The mushroom has been dried and ground in fine powder. The powder was mixed with methanol and distilled water for seven days with a ratio of 1:4 in a glass container. It was then filtered by filtering paper (Whatman size #1). A rotary evaporator has been used to evaporate the solvent to yield the methanol and aqueous extract. These methanol extract *T. versicolor* (METV) and aqueous extract *T. versicolor* (AETV) of were kept in closely sealed glass vials and stored (4 °C) until further use.

2.3. Animals

Either sex of Swiss albino mice at the age of 4–5 weeks old (20–25 g) were procured from BCSIR, Chattogram, Bangladesh.

The mice were kept in room temperature conditions (relative humidity: 55–65% and 12 h light/dark cycle) for seven days to acclimatize with the laboratory conditions. The standard food pellet and water were supplied for the mice through the experiment. However, the study followed the animal guidelines declared by the Swiss Academy of Medical Sciences and the Swiss Academy of Sciences. Animals have euthanized according to the Guidelines for the Euthanasia of Animals: 2013 edition (Leary et al. 2013) and approved by the Institutional Ethics Committee of Department of Pharmacy, University of Chittagong approved this research study under the ethical number.

2.4. Experimental design

Either sex of Swiss albino mice was divided into twenty-six groups (control, standard, MEPTV, and AETV) (n = 5). The METV and AETV groups were administered with 200 and 400 mg/kg according to the body weight (BW), and 1% Tween-80 solution (10 mL/kg, BW) was treated for the control group. The diazepam (1 mg/kg/kg, BW, IP) were administrated as the standard drug for the open field test, hole cross test, forced swimming test, thiopental sodium induced sleeping test, hole board test and rotarod test. For the forced swim test, the imipramine (10 mg/kg, BW) was administrated orally.

2.5. CNS depressant activity

2.5.1. Open field test

The mushroom extract's CNS activity was assessed using the protocol of Saleem et al. with the minor modification (Saleem et al. 2011). The four-sided box was (highlighted in black and white) consisted of 60 × 60 × 60 cm³ with 25 equal squares (5 × 5 cm²). As per Section 2.4, each group was treated. After each group treatment, the mouse from each group was immediately employed on the board and observed for 3 min, where the number of squares movement was recorded. Similarly, the square movement was recorded at 30 and 60 min interval.

2.5.2. Hole-cross test

The hole-cross test for CNS activity was assessed by Takagi et al. with a small modification (Takagi et al., 1971). The hole-cross apparatus are made of wood which consists of 30 × 20 × 14 cm³ dimensions and 7.5 cm in height. A hole was located in the centre of the box (3 cm). As per Section 2.4, each group was treated. After each group treatment, the mice were immediately placed on the board (0, 30 and 60 min interval) and observed for 3 min, where the number of hole crossed was recorded.

2.5.3. Forced swimming test

The forced swimming test method was considered for the CNS depressant activity (Emon et al. 2021). As per Section 2.4, each group was treated. Sixty minutes after the treatment, the mice individually placed and positioned on the glass apparatus, which consist of 25 × 15 × 25 cm³ and filled with water (15 cm, 25 ± 2 °C). Each mouse was recorded for six minutes, where the first two minutes are initial adjustments and the last four minutes mentioned as immobile time.

2.5.4. Thiopental sodium-induced sleeping time test

The thiopental sodium-induced sleeping test was used for CNS activity of the METV and AETV (File and Pellow 1985). As per Section 2.4, each group was treated. After Twenty minutes, each mouse individually administered thiopental sodium (40 mg/kg, BW) intraperitoneally (i.p.), which induced sleep. The onset of sleep and prolongation of sleep was recorded for each mouse.

$$\% \text{ effect} = \frac{\text{Average duration of sleep in the test group}}{\text{Average duration of sleep in the control}} \times 100$$

2.5.5. Hole-board test

The hole-board apparatus evaluated the anxiolytic activity of METV and AETV (Yao et al. 2010). The wood apparatus consists of 16 holes (Diameter: 3 cm) in a square chamber ($40 \times 40 \times 25 \text{ cm}^3$), and raised from the floor at 25 cm. According to Section 2.4., the dosing treatment of each mouse was followed. After 30 min of the administration, each mouse was individually placed and positioned in the centre of the apparatus and recorded the head dipping in the hole for 5 min.

2.5.6. Rotarod test

The rotarod apparatus evaluated the CNS activity by following the earlier described Dunham et al. (Dunham et al. 1957). This research was conducted with a rotarod device, which has a four-section design. According to Section 2.4., the dosing treatment of each mouse was followed. After treatment, each mouse was individually placed in the apparatus at 30, 60 and 90 min at a speed of 12 rpm.

2.6. Antioxidant activity by DPPH scavenging assay

DPPH scavenging assay was incorporated for the Antioxidant activity of METV and AETV (Alam et al. 2020). Two millilitres of serially diluted concentrations (12.5, 25, 50, 100, 200 and 400 $\mu\text{g/mL}$) of METV, AETV and ascorbic acid were mixed with 3 mL of a 0.004% DPPH solution (4 mg DPPH in 100 mL of 95% methanol) and kept them in the incubator for 30 min at 25 °C. The study was followed in a triplicate manner and the absorbance was taken in 517 nm.

Scavenging activity (%)

$$= \frac{\text{Absorbance of Control} - \text{Absorbance of test sample}}{\text{Absorbance of Control}} \times 100$$

2.7. Cytotoxic activity

The cytotoxicity activity of METV and AETV were assessed by brine shrimp lethality bioassay as described by Meyer et al. 1982 (Meyer et al. 1982). By mixing 38 g of sodium chloride (NaCl) in one litre of distilled water (DW), the artificial seawater was prepared and pH maintained at 8.0. A serially diluted concentration (50, 100, 250, 500 and 700 mg/mL) was prepared for METV and AETV, while vincristine sulfate used as a standard in different concentrations (0.25, 0.50, 1 and 5 mg/mL). Then, ten mature nauplii were taken in every test tube for each concentration. Every test tube was assessed after 24 h, whereas the number of alive nauplii was counted and recorded.

Mortality (%)

$$= \frac{\text{Number of nauplii taken} - \text{Number of nauplii alive}}{\text{Number of nauplii taken}} \times 100$$

2.8. Molecular docking study

2.8.1. Protein preparation

The three dimensional (3D) structures of four different receptors are downloaded from the Protein Data Bank server in PDB format (Berman et al. 2002). They are potassium channel receptor (PDB ID: 4UJ) (Lenaeus et al. 2014), human serotonin receptor (PDB ID: 5I6X) (Coleman et al., 2016), urate oxidase receptor (PDB ID: 1R4U) (Retailleau et al. 2004) and human estrogen recep-

tor (PDB ID: 1ERR) (Brzozowski et al. 1997). Then, the four receptors were refined and optimized using the force field (OPLS3) of Maestro V11.1 (Roos et al. 2019, Kotha and Kulkarni 2020).

2.8.2. Ligand preparation

Baicalin, quercetin, catechin, *p*-hydroxybenzoic acid and quinic acid were used for the molecular docking study which was identified in earlier reports (Puia et al., 2018). The compound saved from the PubChem database and converted to three dimensional (3D) structures by a force field (OPLS3) of Maestro V11.1 (LigPrep) (Emon et al., 2020a; Kotha and Kulkarni, 2020).

2.8.3. Grid generation and molecular docking

The specific grids for four different receptors were generated using Schrödinger Glide the default parameters were followed (Kotha and Kulkarni 2020). After grid generation, the molecular docking was followed by the standard precession (SP) ligand docking, whereas the Van der Waals scaling factor was 0.80 along with the partial charge cutoff was 0.15 (Friesner et al., 2004, 2006). The interacted score was recorded for each ligand against each receptor.

3. Statistical analysis

The results were indicated in mean \pm standard error mean (SEM). Here, $p < 0.05$ was measured as statistically significant, where two-way analysis of variance (ANOVA, Dunnett's test) was followed by GraphPad Prism (V.8.4. Besides, one-way ANOVA (Dunnett's test) was used for the hole board and forced swimming test.

4. Results

4.1. CNS depressant activity

4.1.1. Open field and hole-cross test

The METV and AETV dose (200 and 400 mg/kg) exposed significant ($p < 0.05$) decreased locomotion effect of mice in the open field, which was marked from the initial observation (0 min), and continuous to last observation (60 min), with the similar remark of standard Diazepam (Fig. 1A). While the hole-cross test unveiled a non-significant ($p > 0.05$) dose-dependent manner decreased hole crossing for both extracts (METV and AETV) and standard Diazepam (Fig. 1B).

4.1.2. Forced swimming test

The result of the forced swimming test was presented in table 1. The AETV at a lower dose (200 mg/kg) exposed significant ($p < 0.05$) decreases in the immobility times after oral administration when compared to a control group (Table 1). In contrast, 400 mg/kg dose of METV showed the maximal effect. Similarly, a significant decrease in immobility times ($p < 0.05$) was observed by standard diazepam (80.71%).

4.1.3. Thiopental sodium-induced sleeping time test

Like the forced swimming test, METV (400 mg/kg) and AETV (200 mg/kg) exhibited decreased behaviour for the onset of sleep. The findings were summarized in table 2. The AETV (200 mg/kg) and METV (400 mg/kg) showed 154.35% and 136.38% of prolongation of sleeping, while the diazepam was 325.09%.

4.1.4. Hole-board and rotarod test

For METV and AETV, the hole-board test exhibited a significant decrease in head dipping compared to the control group, which is a depressive behaviour of mice (Fig. 2A). A similar observation was

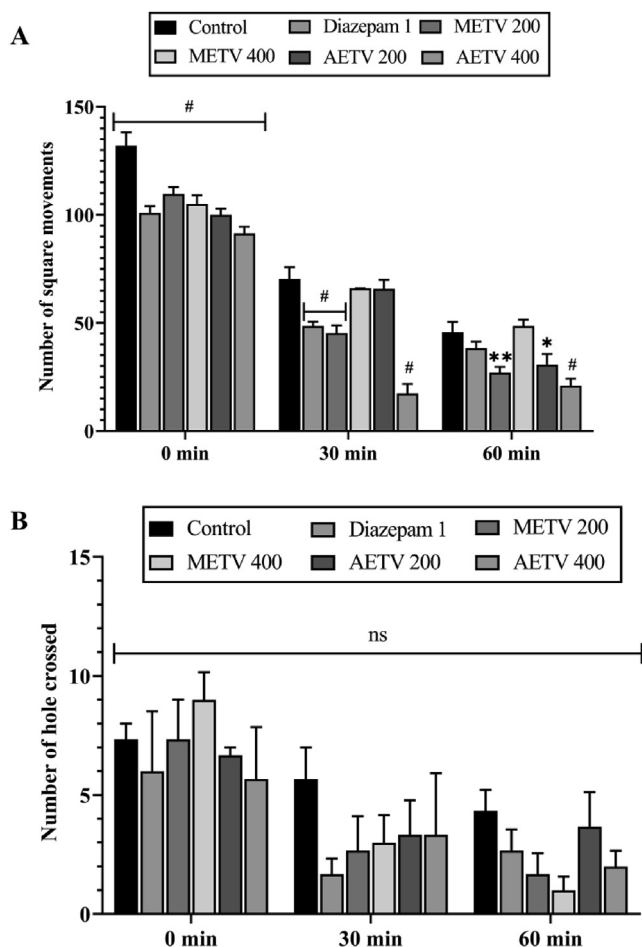


Fig. 1. Effect of methanol and aqueous extract of *T. versicolor* (METV & AETV) on Open field test (A) and Hole-cross test (B). Values are represented as Mean ± SEM (n = 5). * p < 0.01, ** p < 0.05, # p < 0.001 are statistically significant in comparison to Control (10 mL/kg) followed by ANOVA (Dunnett's test).

Table 1

Effect of methanol and aqueous extract of *T. versicolor* (METV & AETV) on forced swimming test in mice.

Groups (mg/kg)	Onset of sleep(min)	% Effect
Control	70.0 ± 7.0	-
Imipramine 10	13.5 ± 1.5#	80.71
METV 200	54.5 ± 12.5	22.14
METV 400	48.0 ± 1.0	31.43
AETV 200	40.5 ± 1.50**	42.14
AETV 400	52.5 ± 2.50	25.0

Values are represented as Mean ± SEM (n = 5). ** p < 0.01, # p < 0.001 are statistically significant in comparison to Control (10 mL/kg) followed by ANOVA.

Table 2

Effect of methanol and aqueous extract of *T. versicolor* (METV & AETV) on thiopental sodium induced sleeping time in mice.

Groups (mg/kg)	Onset of sleep(min)	Duration of sleep(min)	% Effect
Control	30 ± 4.79	44.11 ± 2.13	-
Diazepam 1	7 ± 2.48 #	143.4 ± 5.69#	325.09
METV 200	16.31 ± 6.03	18.28 ± 4.58#	12.75
METV 400	10.71 ± 5.21**	24.93 ± 3.24**	136.38
AETV 200	32.39 ± 1.92	38.48 ± 2.14	154.35
AETV 400	9.68 ± 4.41**	20.63 ± 2.73#	53.61

Values are represented as Mean ± SEM (n = 5). ** p < 0.01, # p < 0.001 are statistically significant in comparison to Control (10 mL/kg) followed by ANOVA (Dunnett's test).

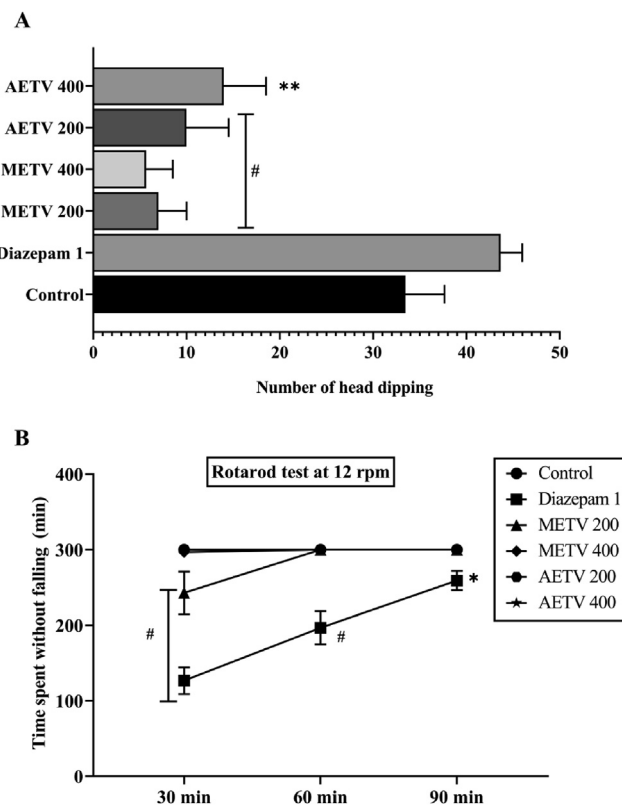


Fig. 2. Effect of methanol and aqueous extract of *T. versicolor* (METV & AETV) on Hole-board test (A) and Rotarod test (B). Values are represented as Mean ± SEM (n = 5). * p < 0.01, ** p < 0.05, # p < 0.001 are statistically significant in comparison to Control (10 mL/kg) followed by ANOVA (Dunnett's test).

exposed by the rotarod test, where a non-significant reduction in time spent by the mice in the rotarod apparatus was observed (Fig. 2B). For both tests, the result of standard diazepam was statistically highly significant.

4.2. Antioxidant activity

Both METV and AETV extract showed a dose-dependent response in the DPPH scavenging assay (Fig. 3). The IC₉₀ value was 178.83 µg/mL, 518.06 µg/mL and 332.98 µg/mL, for METV, AETV and ascorbic acid respectively.

4.3. Cytotoxic activity

METV and AETV extract presented a dose-dependent percentage mortality rate in brine shrimp lethality assay (Fig. 4). The extracts LC₅₀ value was METV = 82.38 µg/mL and AETV = 21.58 µg/mL, while the vincristine sulfate was 0.68 µg/mL.

4.4. Molecular docking study

Catechin demonstrated the highest docking score towards the potassium channel receptor (-5.607 kcal/mol), human serotonin transporter receptor (-8.26 kcal/mol), urate oxidase receptor (-5.847 kcal/mol) and human estrogen receptor (-9.921 kcal/mol). The docking score of Catechin was higher than the standard drugs (Table 3 and Fig. 5).

5. Discussion

The current study was carried out to evaluate the CNS depressant activities of methanol and aqueous extract of *T. versicolor* in

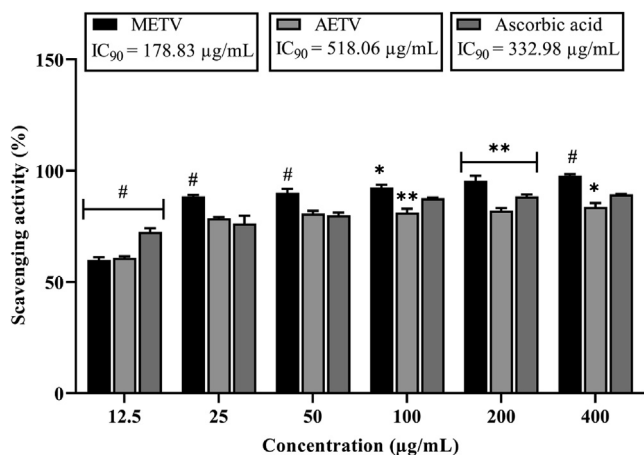


Fig. 3. DPPH scavenging assay of ascorbic acid, methanol and aqueous extract of *T. versicolor* (METV & AETV) on different concentrations. Values are represented as Mean ± SEM (n = 3). * p < 0.01, ** p < 0.05, # p < 0.001 are statistically significant in comparison to Control (10 mL/kg) followed by ANOVA (Dunnett's test).

mice using six neuropharmacological methods, which include open field, hole-cross, forced swimming, thiopental sodium-induced sleeping time, hole-board and rotarod tests. These methodologies are commonly used for neuropharmacological screening models.

The methanol and aqueous extract of *T. versicolor* demonstrated a noticeable decreased in the square movements and crossing of the hole in the open field, and hole-cross tests in mice. The findings indicated that the extract reduced locomotives' activity, which confirms their CNS depressing effects, whereas the open field, and hole-cross test used to assess the locomotor activity. Locomotive behaviour is considered a guide of alertness, and any reduction in locomotion indicates the effect of CNS-depressant (Sousa et al. 2004; Gahlot et al. 2013). This measured the excitability level of the CNS and can be attributable to the CNS depressing effect of the plant extract by reducing motor activity (Mansur et al. 1980; Rakotonirina et al. 2001). Both extracts on the open field, and hole-cross tests reduced the locomotion in the mice substantially. The METV and AETV-treated mice demonstrated a significant decrease in the head-dipping from the hole-board test, suggesting an increased fearfulness. Here, the hole board apparatus assesses the exploratory behaviour of mice individually from the locomotor assay (Takeda et al., 1998; Brown and Nemes, 2008). Earlier, decreased head-dipping behaviour has been described as anxiety behaviour in mice (Saitoh et al., 2006). Several neuro-system (gamma-aminobutyric acid, serotonin, and dopamine) dysregulation might be responsible for anxiety disorders (Murrrough et al., 2015). Motor coordination effect of the extract was observed by rotarod test, whereas the extracts showed a non-significant motor coordination effect which suggesting the antagonistic effect on GABA receptor (Vikas and Payal, 2010; Tirumalasetti et al., 2015), indicating CNS-depressant effect.

Table 3
Docking score of phenolic compounds from *T. versicolor*.

Compounds	Docking score (kcal/mol)						
	4UUJ	5I6X	1R4U	1ERR			
Baicalin	-4.694	-7.858	-4.939	-5.159			
Quercetin	-5.36	-7.131	-5.214	-7.991			
Catechin	-5.607	-8.26	-5.847	-9.921			
p-Hydroxybenzoic acid	-3.904	-4.642	-4.712	-5.89			
Quinic acid	-	-6.595	-5.195	-5.728			
Standard drug							
Diazepam	Imipramine	AA	VS	-3.035	-7.358	-4.512	-

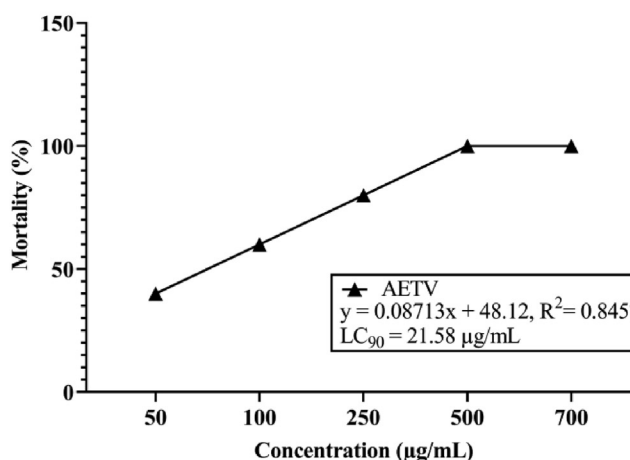
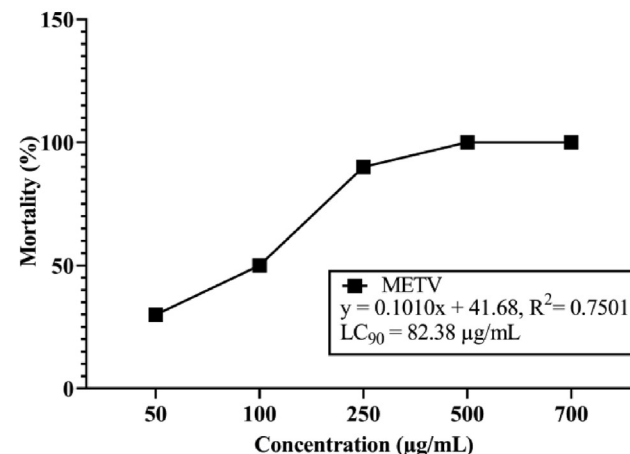
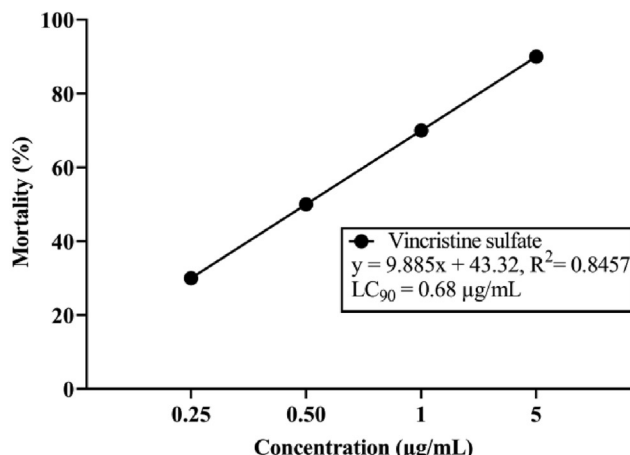


Fig. 4. Brine shrimp lethality bioassay of Vincristine sulfate, methanol and aqueous extract of *T. versicolor* (METV & AETV) on different concentrations.

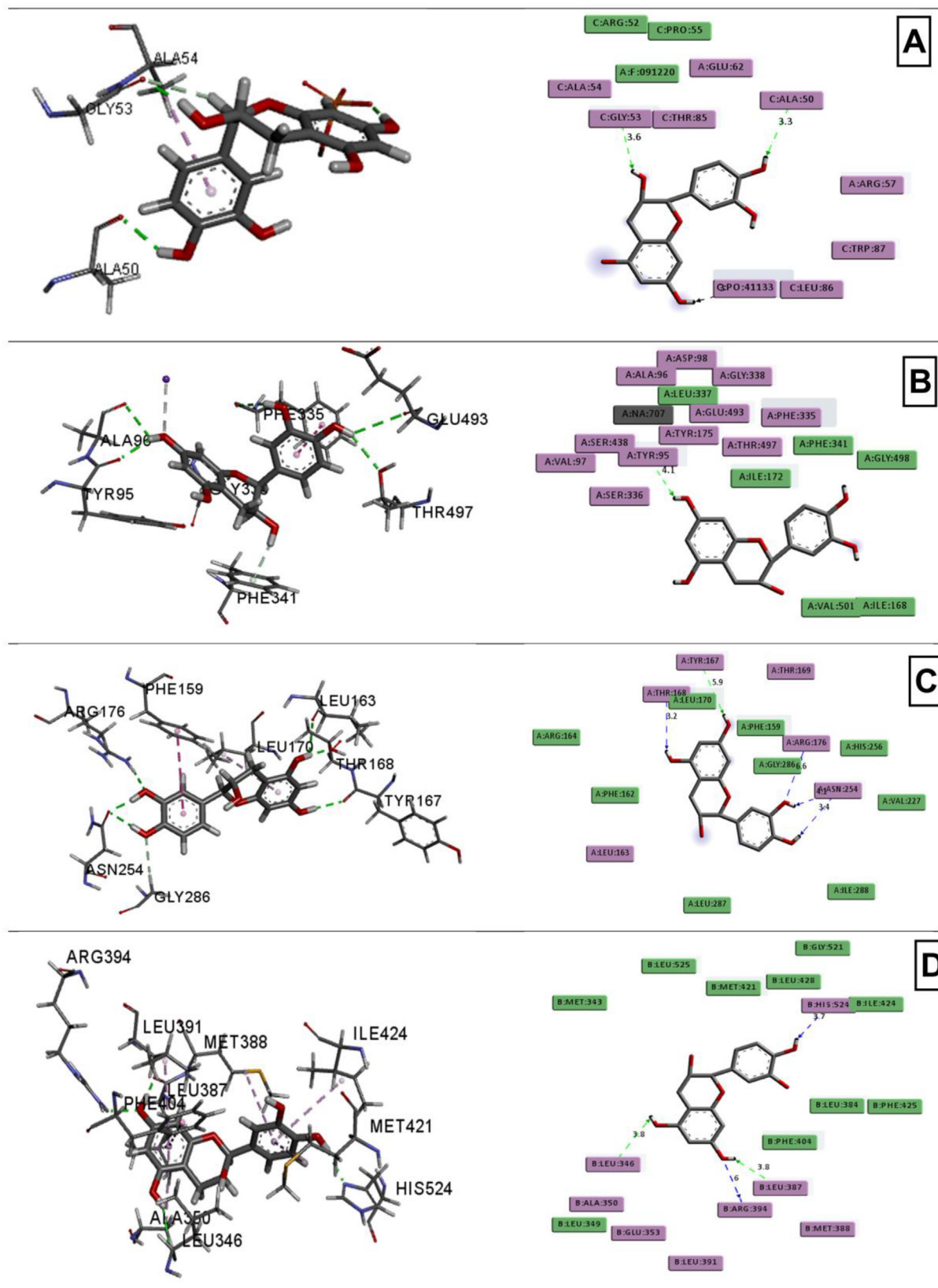


Fig. 5. Molecular docking interaction of phenolic compound catechin towards different receptors. (A) Potassium channel receptor interaction with catechin, (B) human serotonin transporter receptor with catechin, (C) urate oxidase receptor with catechin, and (D) human estrogen receptor with catechin.

The forced swimming test is typically used in rodent models to evaluate antidepressant activity. The decreased percentage in immobility time denotes antidepressant activity, while extended

immobility reflects a CNS-depression response (Subarnas et al., 1993). The lowered concentration of neurochemicals such as dopamine, norepinephrine and dopamine are responsible for

depression. Concurrently, any of the antidepressant drugs act on at least one of these chemical transmitters and increase their activity (Southwick et al., 2005; Berton and Nestler, 2006; Osanloo et al., 2016). The forced swimming test study, in which METV and AETV extract after administration decreased the immobility time in mice, the label that extracts from this plant might increase at least one of the neurotransmitters intricate in depression (Beck and Alford, 2009; Osanloo et al., 2016), while standard diazepam also showed CNS depressant effects on the forced swimming test on mice model. The test for the sleeping time was used to observe sedative-hypnotic drugs in the Swiss albino mouse, while thiopental sodium refers to the barbiturate groups which induce sleep in human and rodent groups (Huang et al. 2007). As such, thiopental induce hypnosis through postsynaptic GABA mediated inhibition initiated by the allosteric modification of the GABA_A receptors. CNS depressant components reduce the onset or duration of sleeping or both (Nyeem et al., 2006; Hasan et al., 2009). Our results unveiled that the higher dose of METV and lower dose of AETV has maximal CNS depressant effect.

Many studies have shown that phenols, flavonoids, saponins, and tannins containing plants help many CNS disorders (Bhattacharya and Satyan 1997), whereas the *T. versicolor* reported 28 phenolic compounds (Puia et al., 2018). This phenolic compound may therefore be mainly accountable for its antioxidant activity. Oxidative imbalance by overproduction of ROS leads to impair the protein and nucleic acids (Zhao et al. 2008). As a result, it causes neuronal dysfunction associated with depressive disorder development (Atmaca et al., 2004; Ng et al., 2008). Although the oxidative condition of antidepressants is improved, their mechanisms of action remain unclear. According to the hypothesis, antidepressants act as a primary or direct effect to restore noradrenergic and serotonergic neurotransmitter systems to normal levels, while antioxidant efforts are a secondary effect (Maes et al., 2000; Tsuboi et al., 2006; Sarandol et al., 2007). Antioxidants are an amazing resource for neutralizing free radicals in lipid chains, which directly convert phenolic groups into stable free radicals that do not trigger further lipid oxidation (Uttara et al., 2009). The METV and AETV have a substantial IC₅₀ value, whereas the METV was higher than the standard ascorbic acid, which could be an alternative approach to treat depression-related disorders.

The polysaccharides from the *T. versicolor* were reported to have a significant toxicity level in the cancer cell. At the same time, they exposed a cell growth inhibitory and apoptosis effect on the cancer cell. According to the recent review by Habtemariam, 2020, the *T. versicolor* has a significant impact on a different cancer cell line, which was studied in several in vitro cancer/tumour cell models and also in tumour-bearing mice models (Habtemariam 2020). Generally, the LC₅₀, which is lower than 100 µg/mL, is signified as highly toxic (Nguta et al., 2011), while in our present study, the METV and AETV reported high cytotoxicity in brine shrimp lethality bioassay.

Computer-Aided Drug Design (CADD) is now an essential tool in the complex process of new drug discovery and development. Simultaneously, molecular docking is a widely known CADD approach that predicts the interaction between the ligands and receptors (Emon et al., 2020b; Rudra et al., 2020). In our present molecular docking study, potassium channel receptor, human serotonin transporter receptor, urate oxidase receptor and human estrogen receptor are used for the CNS, antioxidant and cytotoxicity activities against five phenolic compounds of *T. versicolor*, whereas the catechin showed better and highest docking interaction than other four phenolics and standard drugs. Catechin is a phenolic compound that has neuroprotective effects (Wang et al. 2016). Molecular docking of phenolic compounds of *T. versicolor* towards the different receptors was executed to correlate the observed pharmacological effects with the computational study.

6. Conclusion

The present study displays the analysis of different solvents of *T. versicolor* on CNS depressant activity in mouse models and a significant antioxidant and cytotoxic activity. Five phenolic compounds have interacted with the various receptors, and catechin has shown a strong binding affinity. These effects might be responsible for the phenolic compounds, which require further research.

CRedit authorship contribution statement

S. M. Moazzem Hossen: Conceptualization, Research design, Acquisition, Supervision, Writing - review & editing. **Mohammad Akramul Hoque Tanim:** Research design, Investigation, Formal analysis, Data curation, Software, Writing - review & editing. **Mohammad Shahadat Hossain:** Formal analysis, Data curation, Writing - review & editing. **Saad Ahmed Sami:** Formal analysis, Data curation, Writing - review & editing. **Nazim Uddin Emon:** Research design, Methodology, Validation, Software, Writing - original draft, Writing - review & editing. Finally, all the authors reviewed and agreed to publish this research.

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Competing interests

The authors have no known competing interests.

Ethical Consideration

In keeping with the ethical principles outlined in the Helsinki 2013 Declaration (Emanuel, 2013; Ndebele, 2013) all biological activity evaluation was carried out. The animals were treated in compliance with the values of the Swiss Academy of Sciences and Swiss Academy of Medical Sciences and have been euthanized according to the recommendations for animal euthanasia: 2013 edition.

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