

## Therapeutic Insights and Phyto-chemical Profile of *Kyllinga brevifolia* Rottb: A Review

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<https://dx.doi.org/10.13005/bpj/3096>

(Received: 20 October 2024; accepted: 06 January 2025)

*Kyllinga brevifolia* Rottb. is a perennial herb belonging to Cyperaceae family and is in use in Paraguayan medicinal system as a refreshing beverage with major claims in possessing diuretic, digestive, sedative, tonic, anti-spasmodic and sudorific properties. Information about the herb was gathered through a structured electronic and bibliotheca exploration of different indexed and non-indexed journals and reports published on ethno-pharmacology, phyto-chemistry and traditional applications involving different pre-clinical studies (1972-2024) regarding the evaluation of the effectiveness of the plant. The plant with long slender rhizomes, solitary smooth stem, lanceolate spikelets and radially symmetrical pollen grains is enriched with phyto-constituents like flavonoids (quercetin, vitexin), terpenoids (limonene, linalool, d-cardinene) and steroids ( $\beta$ -sitosterone,  $\beta$ -sitosterol). Various in-vitro and in-vivo scientific evidences unfold the pleiotropic nature of the herb including anti-oxidant, anti-depressant, anti-microbial, anti-aggressive, anti-spasmodic, anxiolytic and sedative property, most of which affect the nervous system. Even some traditional Paraguayan claims in pharmacological properties received controversial scientific output requiring extrapolative experimental confirmatory evidences. However, there is lack of data regarding certain aspects like phyto-constituents responsible for exhibiting effects and accurate molecular mechanism of operation. This comprehensive review summarizes the botanical description, conventional application, phyto-chemistry, pharmacological data and toxicity study of *Kyllinga brevifolia* Rottb. as well as marked novel directions for further research and development to scientifically authenticate the pharmacological capability of the plant.

**Keywords:** Anti-aggressive, Anti-depressant, Anti-spasmodic, Anxiolytic, *Kyllinga brevifolia* Rottb, phyto-constituents.

*Kyllingabrevifolia*Rottb. is a species out of 5,500 plant species belonging to the family Cyperaceae, commonly referred to as sedges. These plants are likely to possess tristichous leaves and unjointed, triangular stems. The genus *Kyllinga* consists of short perennial rhizomes or caespitose annuals with around 40-45 species distributed worldwide around tropical,

sub-tropical, and warm temperature regions<sup>1</sup>. *Kyllingabrevifolia*Rottb. is an invasive perennial herb that multiplies through both vegetative (involving rhizomes and stolons) and asexual means (through seeds that grow into mature plants)<sup>2</sup>. As the plant is a C4 plant, it grows well in regions where the temperature fluctuates between 30 and 35 °C and is probably influenced by low temperature. The herb

emerges in late spring/early summer when a rise in soil temperature is witnessed, grows during the entire summer season and die with the occurrence of the first frost. As the plants develop from the underground rhizome, they are difficult to control at times transforming themselves into invasive weed<sup>3</sup>. According to the record of Dictionary of Chinese Medicine, *Kyllingabrevifolia* Rottb. is sweet, pungent, mildly bitter and neutral in nature. The dosage of 15-30 g for decoction while 30-60 g for fresh products has the capability of eliminating wind, removing heat and blood stasis, cleansing, sustaining blood circulation and reducing pain. The traditional Chinese medicine has the belief that this herb can remove sputum, reduce cough, decline swelling and is mostly in use for the treatment of cold, chill, fever, headache, arthralgia, myalgia, malaria, jaundice, bruises, dysentery and sore swelling. Moreover, in the *Handbook of Barefoot Doctors*, it has been mentioned that the plant can be utilized in the treatment of wind cold after decocted or drank as tea at a dosage of 7-10 g. Likewise, the *Records of Picking Herbs in Lingnan* is of the opinion that it is efficient in the treatment of epidemic fever while in the Paraguayan medicinal traditional system, the rhizomes are utilized as a refreshing beverage and are asserted to have diuretic, digestive, tonic, sedative, sudorific and anti-spasmodic characteristics<sup>4</sup>. The crude hydro-alcoholic *Kyllingabrevifolia* Rottb. extract generated a remarkable elevation in the pentobarbital stimulated hypnotic effect in a dose-proportional manner<sup>5</sup>. The rhizomes of the species present in Brazil are reported to release pleasing fragrance<sup>6</sup>.

## MATERIALS AND METHODS

Information about the therapeutic properties of *Kyllingabrevifolia* Rottb. was gathered through structured electronic (involving PubMed, Google Scholar, Science Direct, Springer, Sci Finder, Wiley Online library, Taylor and Francis and Web of Science) and an in-depth bibliotheca exploration of different indexed and non indexed journals and diverse articles which have been published on ethno-pharmacology, phyto-chemistry and traditional applications. Pre-clinical studies (1972-2024) were taken into account to analyze

the efficacy of the plant. The investigators have applied the ensuing keywords or a combination of the following:-

- *Kyllingabrevifolia* Rottb.
- Medicinal properties
- Phyto-chemistry
- Ethno-pharmacology

## Taxonomic description, habitat and botanical description

*Kyllinga brevifolia* Rottb. is a perennial herb that thrives well in wet grassland, riverbanks and damp areas having an elevation of 5-850 meters and attains a height of about 3-45 cms<sup>3</sup>. The rhizomes of the plant are long, creeping and thin with thickness in the range of 0.5-1 mm while the stem is smooth, green, strongly trigonous and measures 0.5-1.5 mm diametrically. Basal leaves are linear, 1.5-3 mm broad, edged and are shorter than the stem. Flowers are seen from June to October and the flowering pattern was found to bear a coherence with the pattern of average daily precipitation. The fruit structures are obvoid and elliptical while appear double convex lens shaped cross-sectionally with reticulate-tuberculate type surface ornamentation. The pollen grain is radially symmetrical and possesses four apertures with one distal ulceroid aperture<sup>7</sup>. The systematic position is described below:-

Kingdom:- Plantae

Phylum:- Tracheophyta

Class:- Liliopsida

Order:- Poales

Family:- Cyperaceae

Genus:- *Kyllinga*

Species:- *Kyllinga brevifolia* Rottb.

## Pharmacological activity

*Kyllinga brevifolia* Rottb. demonstrates a range of pharmacological properties including anti-aggressive, anxiolytic, sedative, anti-spasmodic, anti-oxidant and anti-inflammatory thereby cementing its position as a medicinal herb.

## Anti-aggressive activity

Aggression is defined as an intended sequence of measures that injures or hurts another organism thereby becoming a serious public health issue worldwide. Aggression is divided into two specific subtypes viz. proactive and reactive aggression in case of clinical terminology. Proactive aggression is hyper-regulated, organized,

predacious and powered by reward contingencies, whereas reactive aggression is commonly marked by an annoyed and spontaneous reaction to a realized threatening incitation with the sole objective of lowering or removing the realized threat. Offensive aggression in animals has numerous characteristics of reactive aggression in human beings such as impulsive responses and neuro-chemical anomalies. A heterogeneous association of social, psychologic and biological factors might be responsible for causing aggression. A correlation of  $\alpha$ -aminobutyric acid (GABA)-ergic neurotransmission in the neurobiology of aggressive behaviour has often been outlined as the agents acting on the GABA<sub>A</sub> receptor complex could be the mediators of aggression<sup>8</sup>. When an experiment involving the determination of anti-aggressive property of hydro-ethanolic (rhizomes) extract (CEKb), hexane (KbF-hex), ethyl acetate (KbF-ethyl-ac), chloroform (KbF-chlo), and aqueous (KbF-aq) extract of *K. brevifolia* Rottb. was evaluated in aggression model in male mice, it was found that the *K. brevifolia* Rottb. [CEKb (10 and 100 mg/kg), KbF-hex (0.1, 1, 10 mg/kg) and KbF-ethyl-ac (0.1, 1, 10 mg/kg)] exhibits anti aggressive-like characteristic in mice as the CEKb is capable of reducing aggressive behavior in a comparable pattern as diazepam (10 mg/kg) while in case of KbF-hex and KbF-ethyl-ac oral treatment, a remarkable lowering in fighting time of isolated mouse was observed. Furthermore, as numerous mechanisms are thought to influence aggression in both non specific (sedation, motor disturbance, psychostimulation) and specific (5-HT<sub>1A</sub>, 5-HT<sub>1B</sub> agonist) ways, henceforth it is not possible to predict the exact mechanism of action of *K. brevifolia* Rottb in exhibiting anti-aggressive behavior (Table 2)<sup>8</sup>. However, further research in this direction could help in deciphering the mechanism and could make the plant a potential medicine for the treatment of aggressive condition in humans.

#### **Anti-oxidant and anti-inflammatory activity**

Methanolic and aqueous *Kyllinga brevifolia* Rottb. extract was found to possess antioxidant properties when evaluated by TEAC assay, reducing power assay, DPPH assay and this might be due to the qualitative phyto-constituents presence while simultaneously disregarding any proportionate quantitative association

between them and the property exhibited<sup>9</sup>. Phyto-constituents like flavonoids possess multiple biological activities like anti-inflammatory and anti-carcinogenic that might be correlated with their anti-oxidant property. Furthermore, the plant possesses three attributes for which it can be used for the treatment, prevention and rehabilitation of Covid-19 viz. capable of efficiently blocking Covid-19 virus from infecting new cells, being able to quickly repair lung damage and is non toxic in nature. The plant is thus capable of resisting Covid-19 infection<sup>10</sup>.

#### **Anti-microbial activity**

Quercetin 3-O- $\alpha$ -apiofuranosyl-(1'12)- $\alpha$ -glucopyranoside 7-O- $\alpha$ -rhamnopyranoside, a quercetin triglycoside isolated from crude hydrophilic *K. brevifolia* Rottb. extract exhibits mild anti-viral activity as 100  $\mu$ g/mL concentration causes a reduction of viral titre of *Herpes simplex virus* type 1 by a factor of 100<sup>11</sup>. The anti-viral activity visualized for this extract might be associated with the presence of still unknown pro-anthocyanidins and polysaccharides. The oral or topical leaf extract administration of the plant is found to be efficacious against viral infections, flu and chest infections (Table 2)<sup>12</sup>.

#### **Anti-spasmodic property**

Though it has been claimed by the Paraguayan traditional medicine that the rhizomes possesses anti-spasmodic property but it has been found that the oral crude hydro-alcoholic extract rhizome administration stimulated a remarkable elevation in the gastrointestinal movement in mice suggestive of the absence of the anti-spasmodic effect (Table 2)<sup>5</sup>. Thus, authentic scientific validation is required in this direction for bringing clarity in the evaluation of anti-spasmodic property.

#### **Anxiolytic and CNS depressant property**

Anxiety is a fundamental indication of several psychiatric abnormalities and is an indispensable element of innumerable medical and surgical conditions. Thus, a common human emotion intimately associated with proper fright and often serve psychobiologically adaptive purposes. The findings from the open-field test, hole-board test, and rota-rod test suggest that crude hydro-ethanolic *Kyllinga brevifolia* rhizome (CEKb) extract administration does not significantly affect the ambulatory (total, central and peripheral) or emotional behaviors like rearing, grooming and

**Table 1.** Overview of pre-clinical studies with *Kyllinga brevifolia* Rottb. regarding the pharmacological properties

Pharmacological Activity	Model	Type of Extract/Compound	Dosage	Observation	References
Anti-aggressive property	Swiss albino mice (male)	Crude hydro-ethanolic extract (CEKb)	Oral dosage of 10 and 100 mg/kg p.o	CEKb causes a remarkable lowering in fighting time of isolated mouse and the reduction in fighting time was reported to be equivalent to that of diazepam (10 mg/kg)	[8]
Anxiolytic and CNS depressant property	Swiss albino mice (male)	Hexane fraction of <i>Kyllinga brevifolia</i> Rottb. (KbF-hex) Ethyl acetate fraction of <i>Kyllinga brevifolia</i> Rottb. (KbF-ethyl-ac) Crude hydro-ethanolic extract (CEKb) Ethyl acetate fraction of <i>Kyllinga brevifolia</i> Rottb. (KbF-ethyl-ac) Crude hydro-ethanolic extract (CEKb)	Oral dosage of 0.1, 1 and 10 mg/kg Oral dosage of 0.1, 1 and 10 mg/kg Oral dosage of 10, 100 and 1000 mg/kg Oral dosage of 10 mg/kg Oral dosage of 1, 10 and 100 mg/kg Oral dosage of 0.1, 1 and 10 mg/kg	Both the extracts cause a remarkable lowering in fighting time of isolated mouse  Both the extracts cause marked elevation in the duration of pentobarbital stimulated sleeping time; The extracts did not modify the hypnosis latency induced by pentobarbital  Both the extracts remarkably elevated the time spent and arm entries into open arms of the elevated plus maze (EPM)	[8]  [13]
Anti-spasmodic property	Swiss albino mice (either sex)	Ethyl acetate fraction of <i>Kyllinga brevifolia</i> Rottb. (KbF-ethyl-ac)	Oral dosage of 100 mg/kg	CEKb stimulated a remarkable elevation in gastrointestinal movement suggestive of no anti-spasmodic property	[5]
Sedative property	Swiss albino mice	Crude hydro-ethanolic extract(CEKb)	Oral dosage of 1, 10 and 100 mg/kg	CEKb causes a lowering of spontaneous locomotor activity, piloerection, passivity, palpebral ptosis, catalepsy, stereotyped behavior and respiration rate and simultaneously causes an elevation in the pentobarbital stimulated hypnotic effect	[11]
Anti-microbial property	mice (male)	Quercetin 3-O- $\beta$ -apiofuranosyl-(1'2)- $\beta$ -glucopyranoside 7-O- $\beta$ -rhamnopyranoside	100 $\mu$ g/mL	Concentration causes a reduction of viral titre of Herpes simplex virus type 1 by a factor of 100	

**Table 2.** Phytochemical constituents of various parts isolated from *Kyllinga brevifolia* Rottb

S. No	Plant part	Phytoconstituents	Class of Phyto-constituents	Country Origin	Ref.
1	Whole plant	Quercetin	Flavonoids	Korea	[7]
2		(-)-epiafzelechin			
3		Vitexin			
4		Orientin			
5	Whole plant	Kaempferol 3-O-apiosyl	Flavonoid glycoside	China	[11]
6		-(1-2)- $\alpha$ -glucoside			
7		Isorhamnetin 3-O—apiosyl	Flavonoid glycoside		
8	Whole plant	-(1-2)- $\alpha$ -glucoside	Flavonoid triglycoside	Korea	[6]
9		Quercetin 3-O- $\alpha$ -apiofuranosyl			
10		-(1'12)- $\alpha$ -glucopyranoside 7-O- $\alpha$ -rhamnopyranoside			
11		$\alpha$ -sitostenone	Steroid		
12	Leaf	Ergosterol peroxide	Steroid	Nepal	[20]
13		$\alpha$ -sitosterol	Steroid		
14		$\alpha$ -sitosteryl-3-O-glucopyranoside	Steroidal Glycoside		
15		Vitexin	Flavonoid		
16		Limonene	Monoterpenoid		
17		1,8-Cineole	Monoterpenoid		
18		Linalool	Monoterpenoid		
19		$\alpha$ -Humulene	Sesquiterpenoid		
20		$\alpha$ -Decalactone	Organic esters		
21		Germacrene D	Sesquiterpenoid		
22		epi-Cubebol	Sesquiterpenoid		
23		$\alpha$ -Muurolene	Sesquiterpenoid		
24		Cubebol	Sesquiterpenoid		
25		$\alpha$ -Cadinene	Sesquiterpenoid		
26		(E)-Nerolidol	Sesquiterpenoid		
27		Germacrene D-4-ol	Sesquiterpenoid		
28		Caryophyllene oxide	Sesquiterpenoid		
29		1-epi-Cubenol	Sesquiterpenoid		
30		$\delta$ -Muurolol	Sesquiterpenoid		
31		$\alpha$ -Muurolol	Sesquiterpenoid		
32		$\alpha$ -Cadinol	Sesquiterpenoid		
33		$\alpha$ -Dodecalactone	Organic esters		
34		(5E,9E)-Farnesyl acetone	Terpenoid		
35	Rhizome and aerial parts	$\alpha$ -thujene	Monoterpenoid	Amazon, Brazil	[6]
36		$\alpha$ -pinene	Monoterpenoid		
37		$\beta$ -pinene	Monoterpenoid		
38		p-cymene	Monoterpenoid		
39		$\beta$ -terpinene	Monoterpenoid		
40		Nonanal	Fatty aldehyde		
41		Myrtenol	Monoterpenoid		
42		Methyl thymol	Monoterpenoid		
43		Methyl carvacrol	Monoterpenoid		
44		Undecanal	Saturated fatty acid		
45		$\alpha$ -copaene	Sesquiterpenoid		
46		$\beta$ -bourbonene	Sesquiterpenoid		
47		$\alpha$ -gurjunene	Sesquiterpenoid		
		2,5-dimethoxy-p-cymene	Ether		
		$\alpha$ -humulene	Sesquiterpenoid		
		Germacrene D	Sesquiterpenoid		

48		Germacrene A	Sesquiterpenoid		
49		á-cadinol	Sesquiterpenoid		
50		Manoyl oxide	Diterpenoid		
51		13-epi-manoyl oxide	Diterpenoid		
52		11-oxo-manoyl oxide			
53		11á-hydroxymanoyl oxide	Diterpenoid		
54		11á-hydroxy-13-epi-manoyl oxide			
55		1â-hydroxymanoyl oxide	Diterpenoid		
56	Aerial parts	â-elemene	Sesquiterpenoid	Amazon, Brazil	[6]
57		Caryophyllene oxide	Sesquiterpenoid		
58	Rhizome and	Cyperene	Sesquiterpenoid	Hawaii, USA	[21]
59	Roots	â-elemene	Sesquiterpenoid		
60		Caryophyllene	Sesquiterpenoid		
61		á-Humulene	Sesquiterpenoid		
62		â-Cadinene	Sesquiterpenoid		
63		Calamenene	Sesquiterpenoid		
64		Patchoulene	Sesquiterpenoid		
65		E-nerolidol	Sesquiterpenoid		
66		â-copaene	Sesquiterpenoid		
67		â-Selinene	Sesquiterpenoid		
68		C <sub>17</sub> H <sub>36</sub>	n-paraffin		
69		C <sub>14</sub> H <sub>40</sub>	n-paraffin		
70		C <sub>23</sub> H <sub>48</sub>	n-paraffin		
71		C <sub>25</sub> H <sub>52</sub>	n-paraffin		

defecation in mice. This indicates that the CEKb extract does not cause sedative or stimulatory effects on locomotor activity or emotional behavior at the tested doses. The lack of changes in these behaviors supports the idea that CEKb has a specific anti-aggressive effect without inducing general behavioral disturbances or impairing motor coordination in mice. Oral dosages of CEKb (10, 100 and 1000 mg/kg) and KbF-ethyl-ac (10 mg/kg) elevated the span of the pentobarbital stimulated sleeping time while CEKb (1, 10 and 100 mg/kg) and KbF-ethyl-ac (0.1, 1 and 10 mg/kg) remarkably enhanced the time-spent and arm entries into open arms of the elevated plus maze (EPM). Moreover as the pentobarbital-stimulated hypnosis latency was not remarkably altered with either dosage of *K. brevifolia* Rottb extracts viz. CEKb and KbF-ethyl-ac which is in turn indicative of the fact that both these extracts might have a CNS depressant activity (Table 2)<sup>13</sup>.

#### Anti-depressant property

Depression is a common, devitalizing, deadly illness with enhanced susceptibility in present day world thereby transforming itself into a enormous health problem. Depressive disorders affect approximately 11.3 % of the adults every

year. While the evaluation of anti-depressant property of CEKb and the KbF-ethyl-ac from *K. brevifolia* Rottb. rhizome on male mice was performed using the forced swimming test (FST) in acute, short term and chronic modalities, it was found that single dosage of CEKb (1.0, 10.0 and 100.0 mg/kg, p.o) and short term oral administration (7 days) with dosage of 10.0 and 100.0 mg/kg/day caused a remarkable reduction in immobility time. Moreover, long term treatment (14 days) with the extract (1.0, 10.0 and 100.0 mg/kg, p.o) resulted in statistically remarkable lessening of the immobility time in FST. Comparable outcome was being visualized with KbF-ethyl-ac (acute dosage of 1.0, 10.0 mg/kg, p.o; short term oral dosage of 1.0 and 10.0 mg/kg and chronic long term dosage of 0.01, 0.1, 1.0 and 10.0 mg/kg). The effectiveness and strength were higher with continued treatment with CEKb and quite unexpectedly, the effectiveness of 14 day treatment of KbF-ethyl-ac (1.0 mg/kg) was comparable to that of imipramine. KbF-ethyl-ac extract when subjected to LC-MS analysis revealed the presence of phyto-compounds like (epi)galocatechin, galocatechin, (epi)afzelechin, (epi)afzelechin, (epi)catechin-(epi)afzelechin, and (epi)afzelechin or afzelechin and it has been

hypothesized that these compounds might be responsible for the possession of aforementioned property by the extract<sup>14</sup>.

#### **Diuretic, Digestive, Refreshment and Carminative property**

The rhizomes of eight to ten plants of *Kyllinga brevifolia* Rottb. are sold as a bundle, crushed in cold water for 'terere' and are used as diuretic<sup>4</sup>. The crude hydro-alcoholic rhizome extract when investigated for the acute toxicity test in mice revealed that it possesses high LD<sub>50</sub> values which is reflective of very low toxicity for both intraperitoneal and oral dosage<sup>5</sup>. This very characteristic might be correlated with its traditional application as a refreshing beverage('terere')<sup>4</sup>. The aromatic leaves and rhizomes of *Kyllinga brevifolia* Rottb. have been reported to function as carminative and digestive as well.

#### **Sedative property**

The intraperitoneal *Kyllinga brevifolia* Rottb hydro-alcoholic rhizome extract administration in mice causes decrease in everyday activity, spontaneous locomotor activity and the rate of respiration. The 1, 10 and 100 mg/kg, p.o. dosage generated remarkable elevation in the hypnotic effect stimulated by pentobarbital in a dosage-dependent pattern. These effects of the extract are indicative of its sedative property that might be attributed to the presence of flavonoid glycosides<sup>5</sup>. While it has also been hypothesized that the sedative property might be correlated with the interplay with benzodiazepine receptors as numerous benzodiazepines and associated compounds are already recognized in distinct plant extracts that attach themselves to the CNS receptors<sup>15</sup>.

#### **Phyto-constituents**

The leaves, roots, rhizomes and in fact the whole plant, *Kyllingabrevifolia*Rottb. is enriched with phytoconstituents ranging from flavonoids to steroids to terpenoids (monoterpenoid, diterpenoid and sesquiterpenoid). The species in various parts of the world exhibit slight variation in the proportion of these constituents as the species from Amazon, Brazil had predominantly oxygen rich diterpenoids from labdane group of compounds while the one from Hawaii, USA demonstrated the presence of C<sub>17</sub> to C<sub>25</sub> n-paraffins along with sesquiterpenoids but similar compounds (sesquiterpenoids) from the samples from both

the countries included  $\alpha$ -copaene,  $\alpha$ -elemene and  $\alpha$ -Humulene<sup>16</sup>. The leaf GC-MS analysis of the species from Nepal had revealed the presence of 22 compounds that are responsible for 96.1 % of the oil composition contributed mainly by  $\alpha$ -cadinol (40.3 %),  $\delta$ -muurolol (19.5 %) and germacrene D-4-ol (12.5 %) along with minor proportions of  $\alpha$ -cadinene (2.9 %) and germacrene D (4.0 %) (Table 1). The Brazilian sample manifested the presence of 13-epi-manoyl oxide (26.1 %) and manoyl oxide derivatives with only 0.4 % of  $\alpha$ -cadinol. Germacrene D was found to be present in comparable proportions between Nepal and Brazil samples (4.0 % and 4.2 % respectively)<sup>6</sup>. The chloroform and n-butanol soluble fractions of *Kyllinga brevifolia* Rottb. from Korea demonstrated the presence of steroids such as  $\alpha$ -sitosterol,  $\alpha$ -sitosteryl-3-O- $\alpha$ -D-glucopyranoside,  $\alpha$ -sitostenone, ergosterol peroxide and flavonoids like vitexin<sup>16</sup>. Another group of Korean investigators revealed the existence of four flavonoids viz quercetin, (-)-epiafzelechin, vitexin and orientin from the whole plant (Table 1)<sup>17</sup>. Two notable flavonoid glycosides [kaempferol 3-O- $\alpha$ -apiosyl-(1-2)- $\alpha$ -glucoside and isorhamnetin 3-O- $\alpha$ -apiosyl-(1-2)- $\alpha$ -glucoside] and a new quercetin triglycoside [quercetin 3-O- $\alpha$ -apiofuranosyl-(1'12)- $\alpha$ -glucopyranoside 7-O- $\alpha$ -rhamnopyranoside] have been found to be isolated from dried and powdered form of the plant from China (Table 1)<sup>11</sup>.

#### **Conservation Status**

The plant is being designated as Least Concern (LC) at both the global and national levels because of its wide spread distribution as it is found worldwide in countries like Europe, China, East Asia, and North America<sup>18</sup>.

#### **Toxicity and side effects**

The intra-peritoneal LD<sub>50</sub> of crude hydro-alcoholic *Kyllingabrevifolia*Rottb. rhizome extract was reported to be 575 mg/kg in 48 hours of inspection while the oral dosage of up to 3.0 g/kg failed to exhibit any lethal symptoms in mice. Furthermore dosage of 1, 10 and 100 mg/kg, p.o. and of 1 and 10 mg/kg.i.p. didnot invoke even mild remarkable alteration in their normal behavior. However, extract dosage of 100 mg/kg,i.p. stimulated a mild lowering in locomotor activity, pilo-erection, passivity, palpebralptosis, catatonia and a stereotyped behavior<sup>15</sup>. While the evaluation

of cytotoxicity of the various *K. brevifolia* Rottb. solvent extracts (hexane, chloroform, ethyl acetate, ethanol, methanol and aqueous extracts) on monkey kidney epithelial (Vero) cells was performed using 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) and neutral red uptake (NRU) assays, the hexane, chloroform, ethanol and methanol extracts were reported to be more lethal to the Vero cells in NRU assay while a strikingly contrasting result was obtained in case of MTT assay as none of the extracts exhibited cytotoxic effect on these cells. Thus, the NRU assay seems to be more susceptible than the MTT assay as the chemical interplay between the plant extracts and MTT seems to hamper with credibility of the MTT assay<sup>19</sup>.

### CONCLUSION

The findings evidenced upon the existing literature reveal *Kyllingabrevifolia* Rottb. as a plant with considerable therapeutic potential. The claims of Paraguayan traditional system of medicine about the exhibition of varied pharmacological properties require authentic scientific validation. Significant gaps exist in the literature in terms of deciphering the relationship between the phyto-chemicals possessed and therapeutic effect exhibited by the plant. Moreover, as the pharmacological effects of the plant are mostly associated with nervous system of the body, the exact molecular mechanism, toxicological studies and proper form of drug administration needs to be figured out using a rigorous systems biology approach. Research to analyze the potentially anti-depressant, anti-anxiety, anti-psychotic or anti-convulsant activities of different solvent fractions in various animal models involving quantitative PCR (qPCR) and western blotting should be undertaken in the future to decode the therapeutic capability of the plant. Even the analysis of molecular interactions (molecular docking studies) between the phyto-compounds and disease-specific biomarker proteins will help understand the underlying mechanism of efficacy exhibition.

### ACKNOWLEDGEMENTS

The authors are thankful to the Head, Department of Zoology, UGC SAP, Bioinformatics

Infrastructure facility, (DBT) Gauhati University for providing the necessary facilities and equipments for conducting the purpose of the study. We also acknowledge Bioinformatics Infrastructure Facility, DST SERB for providing the financial support. The authors acknowledge the DST SERB ECR Grant with Sanction Number: ECR12016/000809 dated 7th March 2017 for provision of financial support.

### Funding Source

The author(s) received no financial support for the research, authorship, and/or publication of this article.

### Conflict of Interest

The author(s) do not have any conflict of interest

### Data Availability

This statement does not apply to this article

### Ethics Statement

This research did not involve human participants, animal subjects, or any material that requires ethical approval.

### Informed Consent Statement

This study did not involve human participants, and therefore, informed consent was not required.

### Clinical Trial Registration

This research does not involve any clinical trials.

### Author's Contribution

Manas Das: Conceptualization, Resources, Supervision, Methodology, Writing-original draft; Aashis Dutta: Data curation, Formal analysis, Methodology, Writing-original draft;

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