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Traditional Uses, Phytochemistry and Pharmacological Aspects of *Rubus niveus* thumb Plant – A Review

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ABSTRACT

Several plant species are utilized in extraordinary common remedy system around the globe and are viewed as doable marketers for the revelation of new medications. Traditional Chinese medication have a long history of flora therapeutically including multiple species of the genus *Rubus* (*Rosaceae*). The pharmacological effects of *Rubus* include antibacterial, antistress, anticancer, antiaging, antiinflammatory, antigastropathic, antirheumatic, antinociceptive, anxiolytic and antiangiardial activities. In India, the roots of *Rubus niveus* (*R. niveus*) are utilized to treat women for excessive menstrual bleeding and its juice extract as an antidote of snake bite. *R. niveus* root helps to relieve rheumatoid pain, clear warmness, detoxify, clear wind damp and deal with dysentery. This review article is focused on the ethanopharmacological, phytochemical and pharmacognostical standardization and pharmacological activity of *R. niveus*.

Keywords: *Rubus niveus*, Pharmacological effect, Antigastropathy, Antirheumatic, Antinociceptive, Anxiolytic.

INTRODUCTION

Plant derived items have a basic natural job against certain pathogenic living beings and are considered as a significant wellspring of present day drugs [1]. Country individuals dwelling in the creation of nations are depending on conventional home-grown therapeutic framework because of their solid acceptance and least access to allopathic drugs [2]. Around 50,000 plant species have been utilized in different traditional medicine system [3,4]. Thus, ethnomedicinal information is helpful for the upkeep of network-based methodologies under this restorative framework. *R. niveus* is an exceptionally intrusive perpetual bush local to India, China and South east Asia. The genus *Rubus* has a significant activity to treat diabetes and some species are reported to produce compounds that exert hypoglycemic, antibacterial, anti-allergic and anti-asthmatic activities [5]. The fruit parts of *Rubus* genus plant are used to makes jams, jellies, pasties, dairy products and juices [6]. *R. niveus* contain a range of biologically active substance including polyphenolics, flavanols, alkanols, anthocyanins, lignans and tannin [7]. *R. niveus* root part used to make soor. Soor is a traditional alcoholic beverage which is used to give strength to the body, act as a blood purifier, anthelmintic and provides relief in urinary troubles [8]. *R. niveus* reproduces sexually through the production of thousands of seeds per bush per year. *R. niveus* has been portrayed as one of the most obtrusive weed species on the Galapagos archipelago and proclaimed as a toxic weed in the territory of Hawaii, USA [9].

Plant profile –Domain (*Eukaryote*), Kingdom (*plantae*), Phylum (*spermatophyte*), Subphylum (*Angiospermae*), Class (*Dicotylendoneae*), Order (*Rasales*), Family (*Rosaceae*), Genus (*Rubus*) Species (*Niveus*)

Preferred common name - Mysore raspberry.

Other scientific name - *Rubus foliolosus* D. Don, *Rubus horsfieldii* Miq, *Rubus lasiocarpus* Sm, *Rubus micranthus* D. Don, *Rubus pedunculatus* D. Don, *Rubus bonatii* H. L., *Rubus boudieri* H. L., *Rubus distans* D. Don, *Rubus godongensis* Y. Gu & W.L. Li, *Rubus incanus* Sasaki ex Y.C. Liu & Yang, *Rubus lasiocarpus* var. *ectenothyrsus* Cardot, *Rubus lasiocarpus* var. *micranthus* (D. Don) Hook. f, *Rubus longistylus* H. L., *Rubus mairei*, H. L., *Rubus mysorensis* F. Heyne, *Rubus pinnatus* D. Don, *Rubus pyi* H. L., *Rubus tongchouanensis* H. L [9].

Distribution –*Rubus* is the most varied genus in plant kingdom, which contains 740 species and these species have been further divided into 12 or 15 subgenera, according to the botanist Daubery (1996) and Jennings (1988). These diverse species are discovered from the top of mountains to coastal location at sea level (Thompson 1995). Some species e.g. Raspberries and black berries have been grown in cool temperate regions of the northern hemisphere, south pacific Islands and are rich in the native *Rubus* species [10].

Taxonomy–

Rubus genus is very complicated to explain with in taxonomical groups due to hybridization, polyploidy, and apomixi [11]. This species is also hard to be distinguished on the basis of phenotypical plasticity. The above drawbacks generate a reason for the development of many biotypes and more than 20 synonyms of *R. genus*. On the basis of economy and ecology all the four crops of *Rubus* genus are beneficial [12]. *R. niveus* is well known as Mysore raspberry. In India it is also called as hill raspberry (Hindi- kala hisalu). It is distributed throughout the temperate Himalayan regions in India, center and western China, Thailand and the Philippine Islands [13].

Ethanopharmacological relevance–

In India *R. niveus* is useful to treat various types of diseases like menorrhagia, its root tips are useful to treat dysentery and diarrhea [14]. Roots and bark mixture is also useful for various types of liver diseases [8,10] and tonic for aged people [15-17].

Phytochemistry –

Various types of chemicals have been isolated and extracted from the *R. niveus* plant which includes phenol, carbohydrate, steroids, saponin, flavonoid, tannin, triterpinoids [18]. On the basis of chemical constituents *R. niveus* is convenient in the treatment of various types of diseases e.g. several kinds of cancers [18], hepatic injuries, wound healing, inflammation etc [19].

Qualitative Phytochemistry analysis–

Dried leaf of *R. niveus* is extracted with purified ethanol in a soxhlet apparatus followed by standard method [20]. (table no 1)

Table 1: Phytochemical analysis of *R. niveus* leaf

S No	Test for	Method	Result
1	Alkaloids	Wagner’s test	Absent
2	Phenol	Ferric chloride test	Present
3	Carbohydrate	Molisch’s test	Present
4	Steroid and sterols	Liebermann reaction	Present
5	Glycoside	Keller – killiani test	Absent
6	Lactone ring in steroidal nucleus	Legal’s test and Baljet’s test	Absent
7	Saponin	Foam test	Present
8	Flavonoid	Alkaline reagent test	Present
9	Tannins	Ferric chloride test	Present
1	Triterpinoids	Salkowski’s test	Present
1	Protein	Ninhydrin test	Absent

Mineral content has also been calculated from the *R. niveus* berries including macro and micro minerals [21].

1)- Macro minerals (mg/100 g on dry weight) contentment in *Rubus* berries.

Micro mineral content (mg/100 gm) of K, N, P, Na, and Ca are 720 ± 0.59, 500 ± 0.06, 1.48 ± 0.02, 56.3 ± 0.05, 390 ± 0.06, and 179 ± 0.89 respectively.

2)-Micro minerals (mg/100 gm on dry weight) contents in *Rubus* berries

Micro minerals content (mg/100 gm) of Fe, Zn, Cu, Pb, Mn, and Cr are 3.26 ± 0.52, 8.13 ± 0.05, 1.070 ± 0.01, 0.234 ± 0.09, 2.43 ± 0.04, and 0.09 ± 0.01 respectively.

Other nutraceutical values of *R. niveus* berries (g/100) -

The nutraceutical values are as following – the parameters in terms of percentage (g/100 dried weight) their contents are, Moisture (78.56 ± 0.87), Ash (4.37 ± 0.09), Crude Protein (3.28 ± 0.87), Crude lipids (1.10 ± 0.07), Crude fibers (5.90 ± 0.25), Carbohydrate (85.35 ± 0.25), and Energy values in Kcal (364.42 ± 0.56).

Active chemical constituent in genotype of *R. niveus* [14] (table no 2).

Table 2: Active chemical constituent in genotype of *R. niveus* fruit

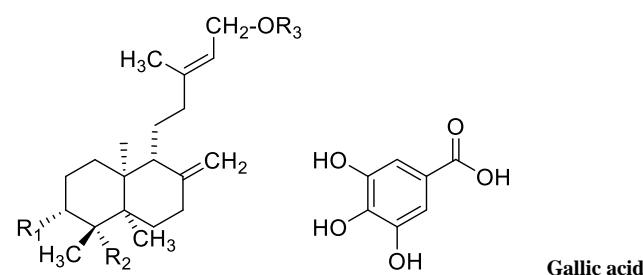
S No	Chemical	Content
1.	Total Phenolic content	3.21 ± 0.06
	• Gallic acid	• 6.59 ± 0.09
	• Catechin	• 12.31 ± 0.17
	• Chlorogenic acid	• 6.15 ± 0.22
2.	Total flavonoid content	4.91 ± 0.18
3.	Total monomeric anthocyanin content	5.63 ± 0.28
4.	Ascorbic acid	10.23 ± 0.02

Some other chemicals have also been isolated from the *R. niveus* including terpinoids, flavonoids, phenylpropanoids, phenols, and some other compounds [14,18]. (table no 3).

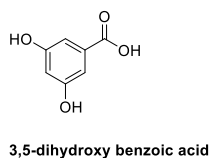
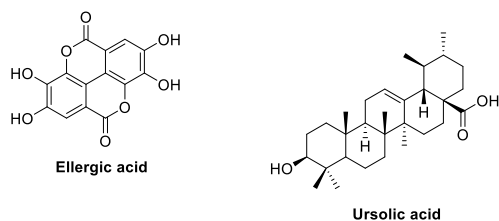
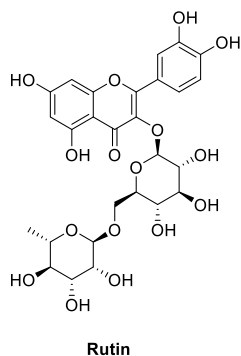
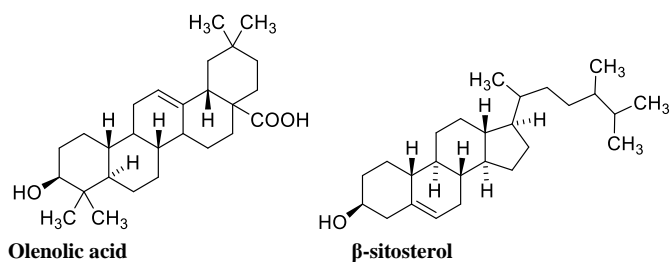
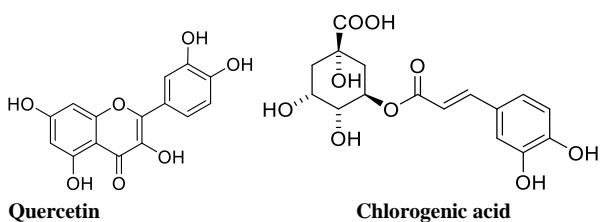
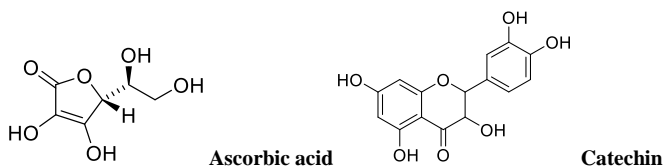
Table 3: Various chemical constituents in *R. niveus*/ foliolosum plant with references

S. No	Isolated chemicals	Ref no.
1.	Oleanolic acid	[22]
2.	Goshonoside F1, F2,F3, F4, F5, F6, F7.	[15, 23, 24, 25]
3.	β- sitosterol.	[22]
4.	Gallic acid	[22]
5.	3,5-Dihydroxybenzoic acid	[22]
6.	ellagic acid	[18, 19]
7.	Quercetin	[26, 27]
8.	Tannic acid	[18]
9.	Rutin	[18]

Goshanoside-



Goshanoside	R1	R2	R3
F1	OH	OH-CH ₂	Glc
F2	OH	GlcO-CH ₂	H
F3	H	COO-Glc	Glc
F4	H	Glc-CH ₂	Glc
F5	OH	GlcO-CH ₂	Glc
F6	OH	Ara (1 → 6) GlcO-CH ₂	H
F7	GlcO	Me	Glc



These chemical constituents are responsible to treat various types of diseases- ursolic acid, quercetin and quercetin derivative are useful to treat various type of diseases e.g- antiproliferative activity of apple peel against human liver, breast, and colon cancer cell lines. Antioxidant activity, antiedema, anticarcinogenic, anti-thrombotic, cytoprotective and anti-bacterial effects, gastric lesions, anti- inflammatory, wound healing etc.

Traditional uses of *R. niveus* / *foliolosus* –

Decauction of *R. niveus* root is helpful to treat cold & cough, headache, fever, dyspepsia, tonsillitis, vertigo/dizziness and enervate period [14]. Fruit part is also beneficial in the treatment of headache [28] useful for human health and nutrition in both ancient and modern times [23]. Root and inner bark infusion are helpful to treat jaundice [29]. Root relieves rheumatoid pain, clear heat and detoxify, clear wind damp, treat dysentery [13,23]. Freshly root tip helps to treat menorrhagia [29], Antigastropathy [30] and also effective as an antidote of snake bite [31,32].

Pharmacology –

Pharmacological activities include Anti-inflammatory, Analgesic, and Antipyretic properties of *R. niveus* root acetone extract, antioxidant activity of hill raspberry etc. Antitumor and wound healing activities are also shown by the *R. niveus* plant.

Anti-inflammatory activity [33]

The various factors are responsible for inflammatory activity e.g- cytokines and chemokines, for which anti-inflammatory therapy is very productive. Many chemicals are capable to treat inflammation which is present in *R. niveus* plant e.g- Oleanolic acid and its derivative [34-40]. Many other researchers also reported anti-inflammatory activity of *R. niveus* plant [41]. B.P George evaluated acute anti-inflammatory activity from acetone root extract of *R.niveus* by the help of two different modified methods these are carrageenan induced rat paw edema [42], and croton oil induced inflammation [43]. Carrageenan has property of inducing acute inflammation. Acetone root extract of different concentration (200 and 400 mg/kg) had been administered orally and Indomethacin (20 mg/kg) was taken as standard drug. Which resulted in the significant effect P<0.05, P<0.01 and P<0.001 respectively. Acetone root extract also showed a significant effect against the Croton oil induced inflammation and significantly reduced the edematous response by using 23.14% 200 mg/kg (p<0.05) and 54.53% 400 mg/kg (p<0.001) respectively.

Analgesic activity [33]

Rubus species contain many chemicals which are helpful to relief pain [44]. The central and peripheral analgesic activities were performed by using two distinctive animal models- acitic acid induced method [45] and hot plate method [46]. Root extract of *R. niveus* showed significant effect at different dose concentration of 200 mg/kg and 400 mg/kg which is P<0.01 and P<0.001 and percentage inhibition 37.31% and 50.75% respectively by using acitic acid induced method. Hot plate method is also convenient to evaluate the analgesic activity, root extract of *R. niveus* gives significant effect resulted in the inhibition of extracted compound by cyclooxygenase and lipoxygenase.

Antipyretic activity [33]

Antipyretic activity of *R. niveus* root extract was evaluated by the yeast induced hyperpyrexia model. The S.C injection of 20 ml/kg body

weight of 15% aqueous suspension of Brewer's yeast injected on the back below the nape of the neck of rat. Yeast induced pyrexia was induced significantly. Paracetamol was taken as a standard drug for antipyretic activity. Rectal temperature had checked after 18 hours interval of standard drug administration. The yeast induced pyrexia was evaluated and then treated with the root extract of *R. niveus* at 200 mg/kg and 400 mg/kg which manifested significant decrease in the rectal temperature of rat and after that. Dose dependent plant extract and paracetamol were compared with the control at ($P < 0.01$ and $P < 0.001$) respectively that indicates the yeast induced temperature elevation would be observe from 3rd to 7th hour after the treatment [47].

Antioxidant properties

Antioxidant activity of the different parts of *R. niveus* i.e., whole plant, fruit etc has been presented in several articles. Mushtaq ahmad *et al* evaluated the antioxidant activity of *R. niveus* berries with the help of *in-vitro* model of DPPH [48]. When given at different concentrations, *R. niveus* berries shown different levels of antioxidant activity and the calculated percent inhibition of *R. niveus* was then compared with the standard i.e. 50, 100, 200, 400 mg/kg, percentage inhibition were 68.30 ± 0.002 , 74.54 ± 0.001 , 80.38 ± 0.002 and 91.64 ± 0.001 respectively and when it was compared with the standard, the highest percentage inhibition calculated was $400 \mu\text{g/ml}$ [21]. By using *in-vitro* DPPH model, Rezeng caidan *et al*, also estimated the antioxidant activity of ethanol, petroleum ether, chloroform, ethyl acetate, n-butanol, and water extract of *R. niveus* and in this model vitamin C was taken as a standard. Where IC_{50} value of vitamin C was $0.020 \mu\text{g/ml}$, and aqueous solvent exhibited the highest IC_{50} value i.e., $0.108 \mu\text{g/ml}$ [49]. Antioxidant activity of methanolic extract of *R. niveus* was recorded as 2.19 mM by ABTS assay, 22.84 mM by DPPH assay and 2.06 mM AE/100 g fw by FRAP assay [14]. Blassam George performed the antioxidant activity of *R. niveus* root extract by using different solvent systems and evaluated it with the help of *in-vitro* DPPH radical scavenging activity, nitric oxide radical scavenging activity and super oxide radical scavenging activity and also by *in-vivo* model. Root extract of *R. niveus* was found to scavenge the stable free radical DPPH significantly ($P < 0.001$) with an IC_{50} value of $5.68 \mu\text{g/ml}$. Antioxidant effect of root against to superoxide and nitric oxide radicals were also effectively scavenged $100 \mu\text{g/ml}$ of *R. niveus* root acetone extract was found to inhibit 54.48% nitric oxide free radicals when compared to BHT and rutin ($P < 0.001$), and $100 \mu\text{g/ml}$. *R. niveus* root acetone extract give the significant effect, when compared to standard BHA and BHT ($P < 0.001$). In *-vivo* antioxidant effect of *R. niveus* root acetone extracts also evaluated. The GSH, GPx, CAT, and SOD were effectively increased in 100 and 250 $\mu\text{g/ml}$ body wt extract. Antioxidant effect of both concentration when compare to untreated group, GSH level significantly increased in both concentration 100 ($P < 0.05$) and 250 $\mu\text{g/ml}$ ($P < 0.01$) treated group, and other enzyme also give the significant effect at 250 $\mu\text{g/ml}$, when compared to untreated group, GPx ($P < 0.001$), CAT and SOD ($P < 0.05$).

Wound healing properties of acetone root extract [18]

The wound healing properties of *R. niveus* root extract was evaluated by Blassan George and he also examined the oral [50] and dermal toxicity [51]. Two doses were selected for this study i.e. 100 mg/kg and 200 mg/kg. By employing two animal models. Blassan George evaluated the wound healing properties. Ointment base was taken as a standard which contains various ingredients such as hard paraffin, cetosteoryl alcohol, wood fat, and yellow soft paraffin and their quantities were 0.5, 0.5, 0.5, and 8.5 gm respectively [52]. The plant root extract (100 mg and 200 mg) were incorporated on the prepared ointment base in

the concentration of 1% and 2% respectively. As standard drug betadine at 5% (w/w) was taken.

To study the wound healing properties of root extract ointment, the two animal models were used and these are as follows-

- Excision and infected wound model [53,54]
- Incision model [55,56]

Excision and infected wound healing model showed significant effect of the *R. niveus* root extract, where the effect of 2% ointment was faster as compare to 1% ointment. The mean percentage contraction of wound area in the excision and infected model was calculated on, 3,6,9,12,15,18 and 21 post wounding days until complete healing. Both ointment concentration of plant extract manifested their significant effects ($P < 0.05$) and ($P < 0.001$) respectively. For control, standard, 1% root ointment and 2% root ointment the Epithelization periods were 27, 12.62, 17, and 13.09 respectively. The effect of Ointment of 2% root extract was similar to betadine (standard) 91.25% and 100% respectively on 12th day. On the 12th day 2% ointment showed significant effect ($P < 0.001$) which was similar to the standard. Contraction rate (%) of control, betadine, neomycin, ointment base, 1% ointment and 2% ointment were 23.62, 81.20, 100, 38.46, 71.70, and 80.63 respectively. The skin breaking or tensile strength [57] was also evaluated on the 10th day post-operation by the incision wound method. The significant skin breaking properties exhibited by the 1% and 2% of root extract ($P < 0.001$) were greater than the control group. Tensile strength (mean \pm SEM, N/cm²) of control (33.50 ± 1.2), betadine ($67.31 \pm 1.03^*$), normal skin ($70.28 \pm 0.9^*$), 1% ointment ($45.73 \pm 0.8^*$) and 2% ointment ($50.63 \pm 12.02^*$). $P^* < 0.001$ have a significant activity of both concentrations.

Antitumor activity [18]

It was evaluated by the solid and ascites tumor development and with the help of DLA cell lines (10^6 cells/ animal) solid tumor was developed on the right hind limb of swiss albino mice. In this model three different plant concentrations 50, 100, 250 mg /kg were taken. Cyclophosphamide taken as a standard drug. After DLA tumor inoculation all the treatment was given orally at 24 hour and continued once daily for 10 days. Initially the volume of right hind limb was measured using Vernier calipers. The tumor volume was measured every third day and the similar procedure was continued up to 1 month period. For the calculation of volume of tumor, the formula used is $V = 4/3(22/7) r_1^2 r_2$, where; r_1 and r_2 are the radius of tumor of two different planes. To induce Ascites Tumor, EAC cell line (10^6) was administered onto male swiss albino mice (intraperitoneally) [58]. After 24 hours of tumor inoculation the animals were treated with standard and test drugs for the 10 days. After treatment, the effect of all drugs and extract on the animals were checked and the ILS of animals was observed by the help of following formula i.e., % ILS = $(T-C)/C \times 100$ where T and C are the average number of days treated and control animal survived respectively. Results of following activity are presented in table 4 –

Antibacterial activity of ethanol extract of *R. niveus* leaves [20]

By using many Bacteria, Shibu Prasanth CR *et al* evaluated the antibacterial activity of *R. niveus* plant extract (40 mg/ml). The various type of *Rubus* species were collected from Nilgiris, Ooty, Tamil Nadu (India).

Antibacterial activity of *R. niveus* leaf extract against the *S. aureus*, *S. epidermidis*, *P. aueuginosa* and *E. coli* was lower than the standard drug Ampicillin.

Antifungal activity [20]

Shibu Prasanth CR *et al.* also evaluated the antifungal activity of ethanolic extract of *R. niveus* leaf extract.

The antifungal activity of *R. niveus* leaf extract against *C. albicans*, *C. krusei* and *T. lignorum* was lower than the standard drug clotrimazole. there was no significant antifungal activity against *A. flavus*.

Gastroprotective effects of *R. niveus* berries

By using the maceration method with methanol, luiane angela nattar nesello *et al.* evaluated the gastroprotective activity on *R. niveus* berries. The animals used for the experiment were female swiss mice (25-30 gm) and rabbits. The two types of animal models were implemented for the study to evaluate the gastroprotective effect, which are as following [30].

- Acidified ethanol induced acute gastric ulcer [59].
- H^+/K^+ - ATPase activity

For acute gastric ulcer, induced by acidified ethanol (60% ethanol/ 0.3 M HCl (Ulcerogenic solution)). Female swiss mice (25-30 g) were taken. Methonolic extract of *R. niveus* were taken 100 and 300 mg/kg and carbenoxolone (control- 100 mg/kg). After one hour administration of the injurious agent in the presence of atm CO₂ animals were euthinized and then dissected after that animal's stomach were separated by using the EARP image analysis. Software carried out the analysis of the stomach in order to determine the gastric ulcer area (mm²) and histological and histochemistry were evaluated by the subcellular fraction using the standard method. The LOOH and GSH were also measured with the help of standard method [60-62]. Methanolic maceration extract of *R. niveus* berries is a favorable source for antiulcer activity, which is confirmed by the macroscopic and microscopic images of stomach. The images showed the decrease level of epithelial damage exhibited potent gastroprotective effect of *R. niveus*. The different concentrations of *R. niveus* berries extract (100 mg/kg and 300 mg/kg) increased the mucin staining in gastric mucosa. H^+/K^+ - ATPase activity the gastric mucosa of a rabbit was employed for the isolation of the gastric microsomal portion by using standard methods [63]. Luiane angela nattar nesello *et al.* evaluated the *in-vitro* gastroprotective effect of *R. niveus* berries and the berries did not show the gastroprotective effect, so the analysis was supported the hypothesis that the extract exerted gastroprotective acitivity without altering proton pump functions.

Toxicology of *R. niveus*

The evaluation of then oral acute toxicity was done in healthy wistar albino mice (150-180 g) and the mice (25-30 g) must be of either sex with approximately same age. The toxicity study was performed as per OECD guidelines. The dose selection of acetone root extract was 100, 500, 1000, 2000 mg/kg. Following the drug administration, animals were observed or analysed for 14 days. After administration of root extract of *R. niveus*, neither any change seen in the behavior nor in the mortality of animals. This is the indication of safe dose of *R. niveus* which is up to 2000 mg/kg of body weight [18,33]. The dermal toxicity

study was performed in healthy wistar rat (150-250 gm) and the safety dose of the extract was up to the maximum dose of 2000 mg/kg [18].

Genotoxicity study

Flora Tolentino *et al.* evaluated the *in-vivo* genotoxicity of methanolic extract of *R. niveus* aerial part. The plant extract was mixed with 1% tween 80 and one of a kind concentration (500, 1000, 2000 mg/kg) was formulated. The doses selection was done on the basis of acute toxicity studies. In which 2000 mg/kg concentration of extract was saved, OECD (2001, 420) [64]. Two methods were performed to study the genotoxicity, which are following (64) – Comet assay (SCGE) – test evaluation done by the standard method [65,66] and Micronucleus test- performed by the standard method [67,68]. After performing the comet assay and micronucleus test, they discovered the considerable result of *R. niveus* plant extract, in exclusive concentration. Doxorubicin (most potent broad spectrum anthraculine antibiotic) used to treat several types of cancers together with quite a few leukemias, lymphomas and strong tumor and it also has the tendency to induce DNA toxicity or genotoxicity, DNA damage, DNA cleavage, leading to mutation and development of second malignant neoplasm [69,70]. In micronucleus test by using PCE/NCE ratio analysis the cellphone viability was checked in trypan blue stain which confirmed that there was absence of cytotoxicity once in 80% of the treatment. Once this test was used to observe the clastogenicity/aureogenicity of *R. niveus* extract in swiss mice bone marrow. In which no significant decrease PCE/NCE ratio was found in treated group as compare to untreated group. Used to be located in tested companies as evaluate to untreated group, each at 24h and 48h of the treatment. These facts indicated that the extract had no giant effect towards cytotoxic effect, however excessive dose had aneugenic/clastogenic impact on bone marrow of swiss mice. When compare with positive control the frequency of cells at 3 dose extract concentration was reduced at time of exposure.

CONCLUSION

Above review it is concluded that *R. niveus* contains various medicinal and pharmacological properties. It is used traditionally as a medicinal. *R. niveus* has been proved to be effective as wound healing, treating various types of cancer, as analgesic, anti-inflammatory, antipyretic, vertigo, antibacterial, anti-viral, anti-fungal, gastroprotective and antioxidant. Fruit parts of *R. niveus* applicable in food, jams, and jellies, stems and leafs part applicable for decorative purpose and root part applicable for dye and staining. Also, it was clear from literature that plays an important protective mechanism for liver cells and traditionally used to make soor. the presence chemicals constituents of this plant can be used in development of new pharmaceutical preparation, that address largely unmet therapeutic needs in our society.

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Conflict of interest

The authors declare that they have no conflict of interest.

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Abbreviations

ABTS – 2,2'-azino-bis (3- ethylbenzothiazoline-6-sulfonic acid)
 BHA – Butylated hydroxyanisole
 BHT - Butylated hydroxytoluene
 CAT- Catalase
 DLA – Dalton lymphoma ascites
 DNA – Deoxyribonucleic acid
 DPPH – 2,2- diphenyl-1-picrylhydrazyl
 EAC – Ehrlich letre ascites carcinoma
 FRAP – Ferric reducing ability of plasma
 GPx- Glutathione peroxidase
 GSH – Glutathione
 GSH- Glutathione
 IC – Inhibitory concentration
 ILS – Increase life span
 LOOH –Liperoxides
 NCE –Normochromatic erythrocytes
 OECD - Organization for economic co-operation and development
 PCE – Poly chromatic erythrocytes
 SCGE – Single cell gel electrophoresis
 SEM – Scanning electron microscope
 SOD- Superoxide dismutase
 USA - United States of America

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