Review Article

www.ijrap.net

(ISSN Online:2229–3566, ISSN Print:2277–4343)

IN VIVO PHARMACOLOGICAL ACTIVITIES OF UPAVISHA SNUHI (*EUPHORBIA NERIIFOLIA* LINN.): A REVIEW

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Received on: 16/02/22 Accepted on: 10/04/22

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DOI: 10.7897/2277-4343.130364

ABSTRACT

The present article is intended to update the information on *In Vivo* studies of pharmacological activities of Snuhi (*Euphorbia neriifolia* Linn.). Snuhi botanically identified as *Euphorbia neriifolia* Linn. belonging to family Euphorbiaceae is a well-known medicinal plant, envisages to possess numerous medicinal properties. One among the Upavisha, Snuhi, has been attributed with several synonyms depicting its morphological identifying characters and pharmacological activities. Snuhi contains mainly Laghu and Tikshna guna. It is indicated in 25 clinical conditions like Gulma, Udara, Shotha, Vranashotha, Plihavikara, Dushivisha etc. Snuhi has various pharmacological properties such as antibacterial, antioxidant, wound healing, immunomodulatory, and anticancer etc., Various *In Vivo* and *In Vitro* studies have been studied on Snuhi for pharmacological activities. But no independent and concise data is available for *In Vivo* studies of Snuhi. Hence, the present review attempts to encompass the up-to-date comprehensive published *In Vivo* studies on Snuhi with reference to its various pharmacological activities that will be helpful for further clinical research.

Keywords: *In Vivo*, Pharmacological activities, Snuhi, *Euphorbia neriifolia* Linn., Upavisha

INTRODUCTION

Herbal preparations have been used from ancient to the present era and are benevolent to humankind. According to an estimation by the WHO, around 80% of the world's population relies on drugs from plant sources.[1]

Snuhi is one of the potent and beneficial plants in Ayurvedic pharmacopoeia of India.[2] Snuhi is botanically identified as *Euphorbia neriifolia* Linn. and belongs to the family Euphorbiaceae.[3]

Snuhi is one among the Upavisha.[4] Upavisha is a group of less toxic drugs used to cure many diseases. According to Acharya Charaka, even poison becomes an excellent drug if appropriately administered.[5] Snuhi possesses Katu rasa, Katu vipaka, Ushna virya, Laghu- Tikshna guna, Kaphavatahara, Vedanasthapana, Lekhana, Tikshnavirechaka, Raktashodhaka, Shothahara, Kaphanissaraka, Twakadoshahara Karma.[4] These Gunas are responsible for the pharmacological activities of Snuhi.

Pharmacological studies and traditional uses of Snuhi show antibacterial, antioxidant, wound healing, immunomodulatory, radioprotective, anticancer, etc. activities. These pharmacological activities occur due to phytoconstituents like lectin, quercetin, saponin, flavonoids, triterpenes, diterpenes, phlobatannins, alkaloids and glycosides.[6]

As far as the literature survey could ascertain, limited information is available on the *In Vivo* pharmacological activities of Snuhi. Therefore, this article attempts to present a detailed review of the *In Vivo* studies of the pharmacological actions of Snuhi.

A systematic literature search was performed on PubMed, Research Gate, Academia, Nigerian Journal of Experimental and Clinical Biosciences, Indian journal of pharmacology in July-September 2021 to investigate the *In Vivo* studies of pharmacological activities of Snuhi (*Euphorbia neriifolia* Linn.) till date. For this purpose, the following terms, "Pharmacological activities" OR "*Euphorbia neriifolia* Linn." OR "Snuhi" OR "Upavisha" OR "*In Vivo* studies" and combinations were searched in the title, keywords and abstract of articles to find appropriate documents. The pharmacological activities of Snuhi were assessed with clear case definitions of pharmacological activities.

All appropriate documents concerned with *In Vivo* studies of Snuhi were included with no strict inclusion criteria. No time limitation was defined for the selection of eligible articles. However, to avoid misconception as well as to ease data extraction, the exclusion criteria in this review are as follows:

1. Articles with language other than English
2. Documents with duplicated data
3. Editorials, conference papers and review articles
4. Research articles on *In Vitro* studies
5. Research articles on Clinical studies
6. Articles on *In Vivo* studies of other species of Euphorbiaceae family other than *Euphorbia neriifolia* Linn.
7. Articles with insufficient data and irrelevant articles[13]

Literature Review

Table 1: Upavisha Snuhi [3, 6, 7, 8, 9, 10, 11]

Botanical Name	*Euphorbia neriifolia* Linn.
Family	Euphorbiaceae
Vernacular names	Hindi - Thuhara, Sehunda Marathi - Nivadunga English - Common Milk Hedge, Indian spurge Tree
Classification	Ayurveda - Akrutrima, Sthavara, Upavisha Modern Toxicology- Irritant Organic Vegetable Poison
Sanskrit synonyms	Sehunda, Sinhatunda, Vajri, Vajradruma, Sudha, Samantadugdha, Snuk, Guda
Gana	Charaka - Virechana, Shatashodhanavruksha Sushruta - Adhobhagahara, Shyamadi Vagbhata - Nikumbhadi (Virechana)
Rasa	Katu
Vipaka	Katu
Virya	Ushna
Guna	Laghu, Tikshna
Karma	Bahya- Vedanasthapana, Lekhana Abhyantara - Tikshnavirechaka, Raktashodhaka, Shothahara, Kaphanissaraka, Twakdoshahara
Doshaghnata	Kaphavatahara
Rogaghnata	Shoola, Aamadosha, Ashthilika, Aadhamana, Gulma, Udara, Arsha, Shotha, Vranshotha, Jwara, Plihavikara, Dushivisha
Prayojyanga	Kshira, Patra, Kanda, Moola
Types	According to Charaka Samhita – 1) Alpakantaka 2) Bahukantaka
Description	Xerophytic tree or shrub is glabrous erect branched succulent, 20 ft or 1.8- 4.5m high with jointed cylindrical or obscurely 5-angled branches.
Biological activities	Anticarcinogenic, Anti-inflammatory, Antimicrobial, Antioxidant, Antiulcer, Cytotoxicity, Radioprotective, Wound healing Property, Anesthetic, Analgesic, Immunomodulatory etc.
Fatal dose	Uncertain (25 -30ml of latex)
Fatal period	Uncertain (3 days)
Formulations	Chitrakadi taila, Abhyadi vati, Avittoladi bhasma, Vajra kshara

Table 2: Chemical constituents of Snuhi[12]

Powdered plant, stem and leaves	Several triterpenoids like Glut-5-en-3$-ol, Glut 5(10)-en1-one, taraxerol and $-amyrin
Latex	Triterpene- nerifoliene, euphol, neriifoliol, neriifolene, euphorbon, resin, gum, caoutchouc, malate of calcium, monohydroxy triterpene, neriifoliol, taraxerol, beta-amyrion, glut-5-(10)-en-1-one, neriifolione, cycloartenol
Leaf	Friedelan-3, D: B-friedolan-5-(10)-en-1-one, taraxerol
Bark	Euphol, Euphorbol, hexacosanoate, n-hexacosanol, 12-deoxy 4-β-hydroxyphorbol-13-dodecanoate-20-acetate, pelargonin-3, 5-diglucoside, 24-methylene cycloartenol, tulipanin-3, 5-diglucoside
Stem	Euphol, friedelan-3, D: B-friedolan-5-(10)-en-1-one, glut-5(10)-en-1-one, taraxerol
Root	Aluns-5(10)-ene-1-one, anthocyanins, euphol, pururate dikinase, terpenes, 24-methylene cycloartenol, tulipanin-3, 5-diglucoside
Ethanolic extract of fresh root	Antiquorin

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Exploring articles through systematic research provided information which revealed an abundance of variety in the In Vivo pharmacological activities of Snuhi. Data in Table 3 summarises the In Vivo pharmacological activities of Snuhi with respect to plant part used, type of extract, a dose of extract, the animal model used, inducer, specific investigations and findings.

Table 3: *In Vivo* Studies of pharmacological activities of Snuhi (*Euphorbia neriifolia* Linn.)

SN	Pharmacological activity	Plant part used	Type of extract	Dose of extract	Animal model used	Inducer	Special investigations	Findings
1.	Anaesthetic	Stem	Alcoholic extract	5, 10, 20, 40 and 80mg	Frog, Guinea pig	-	Foot-withdrawal reflex in the frog, Intradermal wheal method in guinea pig	In the Foot-withdrawal reflex test, the onset of anaesthesia was 15, 12.5, 12, 8 and 5 min. in the extract-treated group. In the control group, the onset of anaesthesia was 3 min. By intradermal wheal method, the onset of anaesthesia was 2 min and 1 min for 20 and 40mg, respectively. The anaesthetic property of the extract is similar to that of procaine hydrochloride except for the time of duration.[14]
2. i.	Analgesic	Leaves	Hydro-alcoholic extract	400 mg/kg/day	Wistar albino rats	-	Tail flick and Eddy's hot plate method	The extract exhibited a marked central analgesic effect as evidenced by a significant increase in reaction time (increased threshold potential of pain) compared to the control. The results were

								comparable to the standard drug, diclofenac sodium in both methods.[15]
2. ii.	Analgesic	Leaves	Hydro-alcoholic extract	100, 200 and 400 mg/kg	Wistar albino rats	-	Thermal stimulus (Tail flick method, Eddy's hot plate method), Mechanical stimulus and Chemical stimulus	Extract at 400 mg/kg dose showed 432.22% pain inhibition in Eddy's hot plate method after 60 min of drug treatment. An increase in tail-flick and tail clip response 45 min after drug treatment was noted to be 416.36% and 165.94%, respectively, at a 400 mg/kg dose. In this same dose, acetic acid-induced writhing episodes protection was 53.83%.[16]
3.	Antianxiety, Anticonvulsant, Antipsychotic	Leaves	Hydro-alcoholic extract	Pre-treatment with 100, 200 and 400 mg/kg	Swiss albino mice, Wistar albino rats	Diazepam, Pentobarbitone sodium, Apomorphine, Scopolamine Hydrobromid, Chlorpromazine injections i.p.	Anti-anxiety activity on elevated plus-maze in mice, Taming effect on apomorphine-induced stereotype in rats, Study of condition avoidance response in rats, Effect on the extrapyramidal system in rats, Measurement of transfer latency on elevated plus-maze in mice, Screening of anticonvulsant activity.	Extract at all doses reduced apomorphine-induced stereotype and devoid of cataleptic effect, suggesting specific dopaminergic receptor modulating activity. The extract (400 mg/kg) potentiated pentobarbitone-induced hypnosis showed protection against maximal electro-shock-induced convulsion and had anxiolytic action by increasing the percentage of time spent in the open arm elevated plus-maze; it also did not reverse scopolamine-induced amnesia on elevated plus-maze. Extract (200 and 400 mg/kg) increased transfer latency also in combination with scopolamine. These results indicated antianxiety, antipsychotic, and anticonvulsant activity on EN extract.[17]
4.	Antiarthritis	Leaves	Triterpenoid fraction of EN (TFEN)	250 and 500 mg/kg of TFEN for 28 days	Wistar rats	0.1 ml of CFA s/c to sub plantar region of the right hind paw and at the base of the tail	Assessment of arthritis index, measurement of serum TNFα, histopathology of tibia-tarsal joint.	Pre-treatment with two different doses of TFEN significantly reduced paw oedema. TFEN in 500 mg/kg dose significantly reduced the arthritis index compared to CFA alone treated group. CFA control, TFEN and methotrexate, respectively, showed arthritis index values of 4.02, 2.10 and 1.72. The positive result of this study indicates that TFEN has a potent anti-arthritic effect.[18]
5. i.	Anticancer	Leaves	Isolated Flavonoid (ENF), Hydro-Ethanolic Extract of EN (EN)	150 and 400 mg/kg BW/day of EN for 21 days	Swiss albino mice	50mg/kg BW of DENA induction for renal carcinoma	i. Oxidative stress (LPO), ii. Levels of antioxidants (SOD, CAT, GST, GSH), iii. Biochemical parameters (AST, ALT, ALP, TP and TC) iv. Renal markers (urea and creatinine) v. Xenobiotic enzymes (Cyt P450 and Cyt b5)	Pre-treatment with ENF and EN counteracted DENA- induced oxidative stress and exerted its protective effects by restoring the levels of antioxidants, biochemical parameters, and renal markers in renal tissue.[19]
5. ii.	Anticancer	Leaves	Isolated Flavonoid (ENF), Ethanolic extract of EN (EN)	150 and 400 mg/kg BW/day of EN for 21 days	Swiss albino mice	50mg/kg BW of DENA induction for hepato-carcinoma	i. Oxidative stress (LPO), ii. levels of liver markers (AST, ALT, ALP) iii. Levels of antioxidants (SOD, CAT, GST, GSH), iv. Biochemical parameters (TP, TC) v. Xenobiotic enzymes (Cyt P450 and Cyt b5)	Pre-treatment with EN and ENF counteracted DENA- induced oxidative stress (LPO). It exerted its protective effects by restoring the levels of liver markers, antioxidants, biochemical parameters and xenobiotic enzymes in liver tissue.[20]
6. i.	Antidiabetic	Leaves	Ethanolic extracts of *Euphorbia neriifolia* Linn. (ENEE)	200 and 400 mg/kg BW for 21 days	Wistar albino rats	A high-fat diet with Injection Streptozotocin i.p., at a dose of 35mg/kg	Oral glucose tolerance test (OGTT), Fasting Blood Glucose (FBG)	In OGTT, ENEE at a 400 mg/kg dose produced a maximum fall at 60 min after glucose administration. The extracts produced a dose-dependent fall in FBG. Reduction in FBG for Diabetic control, Standard grp and extract at 400 mg/kg was 307.79±3.24, 94.17±1.15 and 127.26±1.43.[21]
6. ii.	Antidiabetic	Leaves	Ethanolic extract	100, 200, 400 mg/kg for 21 and 45 days	Wistar albino rats	-	Serum glucose level	Extract initially at 21 days of treatment had a non-significant effect on serum glucose. On the other hand, after 45 days, extract at 200 and 400 mg/kg showed respectively 82.48±4.60 and 43.23±3.58 reduction of glucose, whereas the vehicle control group showed 112.63±4.68.[22]
7. i.	Anti-inflammatory	Leaves	Hydro-alcoholic extract	100, 200 and 400 mg/kg	Wistar albino rats	1. 0.1ml of 1% w/v Carrageenan (for induction of paw oedema) 2. Cotton pellet induced granuloma	The volume of the paw (by mercury displacement technique using plethysmometer), percentage inhibition in paw oedema volume	The Wistar rats model showed 69.47 and 75.78% inhibition of oedema volume, respectively, by extract (at 400 mg/kg dose) and aspirin. The same dose of extract and diclofenac showed 60.61 and 66.14% inhibition of granulomatous tissue mass development recognised by the cotton pellet-induced granuloma model.[16]
7. ii.	Anti-inflammatory	Leaves	Hydro-alcoholic extract	Pre-treatment with 400 mg/kg	Wistar albino rats	0.1 ml of 1% w/v Carrageenan into sub plantar	Mean paw volume (using plethysmometer), Percentage	Anti-inflammatory effects of the hydro-alcoholic extract were observed and found to be significant at P<0.001. The per cent inhibition in paw oedema after 3h was

						region of the right hind paw of rats	inhibition in paw edema volume	recorded at 63.27% in the case of indomethacin (standard) and 55.12% in the extract.[15]
7. iii.	Anti-inflammatory	Latex	Petroleum ether fraction	Pre-treatment with 500 and 750 mg/ml local application	Wistar albino rats	0.1 ml of 1% w/v Carrageenan solution in normal saline was injected beneath the sub-plantar surface of rt. hind paw	The volume of paw before and 3 hrs. after carrageenan treatment (using plethysmometer), Percentage inhibition in paw oedema volume	Topical latex pet. Ether fraction at 750 and 500 mg/ml dose showed 42.40 and 35.25% inhibition of carrageenan-induced paw oedema compared to 71.22% inhibition of topical diclofenac sodium (100 mg/ml).[23]
8. i.	Antilipidemic	Leaves	Ethanolic extract	200, 400 mg/kg for 15 days	Sprague Dawley rats	A high-fat diet with Injection Streptozotocin i.p., at a dose of 35mg/kg	Serum lipid profile	Treatment at 400 mg/kg increased Sr. HDL cholesterol to 44.07±1.17 mg/dl, whereas the normal control showed 52.85±2.22 mg/dl. The same treatment decreased Sr. TC, LDL, VLDL at 73.0±1.57, 53.56±1.26 and 35.54±0.99 mg/dl, respectively, whereas the normal control showed 62.84±1.67, 34.03±1.84 and 25.73±1.39, respectively.[21]
8. ii.	Antilipidemic	Leaves	Ethanolic extracts	100, 200, 400 mg/kg for 21 and 45 days	Wistar albino rats of both sex	-	Serum biochemical parameters	Extract at 400 mg/kg reduced serum lipid profile including cholesterol (as 73.23 ±3.16 mg/dl), triglyceride (as 42.21±2.76 mg/dl) and LDL (as 4.43±0.16 mg/dl) where the vehicle control group showed 104.72±5.17, 65.17±3.07, 46.29±2.12 mg/dl, respectively after 45 days treatment. Also, increased serum HDL at 400 mg/kg dose.[22]
9.	Antioxidant	Leaves	Ethanolic extract	100, 200, 400 mg/kg for 21 and 45 days	Wistar albino rats of both sex	-	Liver and kidney antioxidant enzyme parameters, Thiobarbituric acid reactive substances assay	Liver lipid peroxidase was decreased (7.78±0.69 nmol/mg of protein) after 45 days of treatment of extract (400 mg/kg) compared with vehicle control (29.94±1.22 nmol/mg of protein). Extract at 200 mg/kg increased the level of SOD by 26.06±1.22 unit/mg of protein in the liver and 47.58±2.24 unit/mg of protein in the kidney. In contrast, the vehicle control group showed only 1.76±0.23 unit/mg of protein in the liver and 4.31±0.69 unit/mg of protein in the kidney, respectively, after 45 days of treatment.[22]
10.	Antiulcer	Leaves	Hydro-alcoholic extract	Pre-treatment with 100, 200 and 400 mg/kg	Wistar albino rats of both sex	1. Pyloric ligation-induced gastric ulceration 2. Ethanol-induced gastric ulceration	Ulcer index, Ulcer grading, Gastric content biochemical analysis	Extract at 200 and 400mg/kg decreased ulcer index, ulcer grading and free acidity. However, there was a significant decrease at 400 mg/kg in gastric content's total acidity and volume.[16]
11.	Diuretic Activity	Leaves	Hydro-alcoholic extract	100, 200 and 400 mg/kg	Wistar albino rats of both sex	-	Urine output along with electrolyte concentration	EN extract showed dose-dependent diuretic activity, which was highly significant at 400mg/kg. Fifth-hour urine volume for 400 mg/kg dose was 17.45 ml compared to 6.65 ml of control.[16]
12.	Immuno-Modulatory	Leaves	Hydro-alcoholic extract	100, 200 and 400 mg/kg/day of bw for 14 days	Wistar albino rats of either sex	1. Abdominal sepsis caused by E. coli in all groups. 2. 1mg/kg BW of beta-methasone i.v. for immune suppression.	Survival study of E. Coli induced Abdominal sepsis in rats, haematological parameters, phagocytic Index, humoral immune response, cell-mediated immune response	In E. coli induced abdominal sepsis control, control with betamethasone, extract (400 mg/kg) and extract with betamethasone treatment showed 66.6%, 100.0%, 16.6% and 33.3% mortality after 48 hours of treatment, respectively. Phagocytic index was found to be 0.0127, 0.0286, and 0.0252 respectively for control+ betamethasone, extract (400mg/kg), and extract+ betamethasone. Extract remarkably potentiates hem-agglutination antibody titre and cell-mediated immunity by facilitating the footpad thickness response in normal and betamethasone induced immunosuppressed rats. The extract also increased TLC and DLC in immunosuppressed rats.[24]
13. i.	Hepatoprotective	Leaves	Saponin fraction (ENSF)	50, 125, 175 mg/kg for 7 days	Wistar albino rats of both sex	Carbon tetrachloride 1.5mg/kg i.p.	Thiopentone induced sleeping time, Sr. biochemical parameters, Histopathological studies of liver, Estimation of the free radical scavenging ability of the liver, Viability study of liver, Bromsulphalein uptake test.	ENSF reduced the sleeping time to 24.25±1.62 min compared to 65.72±2.43 min of negative control at 175 mg/kg. Pre-treatment with ENSF attenuated the acute increase in sr. SGPT, SGOT, ALP activities and considerably reduced the histopathological alterations. The extract improved the antioxidant status of the liver by an increase in SOD and Glutathione. Silymarin, negative control and ENSF at 175 mg/kg dose showed the viability of liver cells as 87.89, 61.56 and 82.93%, respectively. Liver slices of ENSF treated animals showed extremely significant hepatoprotection (54.33%) at a 175 mg/kg dose. It showed 75.44±4.12 µg of bromsulphalein uptake per gram of liver tissue compared to 42.11±2.38 µg of the CCl_4treated group.[25]
13. ii.	Hepatoprotective	Leaves	Ethanolic extracts	100, 200, 400 mg/kg for 21 and 45 days	Wistar albino rats	-	Sr. biochemical parameters	Treatment of 45 days decreased SGOT as 45.55±3.71 and 8.31±0.85 of vehicle control and extract(400mg/kg). Increase in level of ALP as 68.24±3.84 and

								138.97±5.61 U/l of control and extract(400mg/kg) on 45 days treatment.[22]
14. i.	Wound healing property	Leaves	Ethanolic extract	100, 200, 400 mg/kg p.o. for 21 days	Wistar albino rats	Excision of total thickness skin from the dorsal thoracic central region to get 500mm^2 wound under anaesthesia.	Wound contraction and epithelisation period in an Excised wound, Determination of hydroxyprolin, protein, catalase and superoxide dismutase in wound granulation tissue.	Wound epithelization days were 22.50±1.22, 18.15±1.34, 16.45±0.94 for control, extract (400mg/kg) and vitamin c treated group respectively. Granulation tissue wt. 36.83 mg, 147.24 mg and 165.60 mg for control, extract (400mg/kg) and ascorbic acid-treated group. A significant increase in hydroxyproline content, catalase activity and a decrease in superoxide dismutase activity in granulation tissue in the extract-treated group evaluates the wound healing activity of the extract.[26]
14. ii.	Wound healing property	Latex	0.5% and 1% Aqueous extract	20µl L/A twice a day for 4 and 7 days	Guinea pigs	Cutaneous circular wounds of 8 mm were inflicted on the dorsal surface of an animal under anaesthesia.	Measurement of the surface area of the wound, Measurement of tensile strength, Histopathological studies, Biochemical parameters (DNA and Protein levels, Hydroxyproline estimation).	The 1% treated wound area was reduced by 18 and 30% on days 4 and 7. The decrease on the 7th day was found to be significant. Tensile strength, DNA, and Hydroxyproline were 358±22g/cm^2, 12.41±0.65mg/g tissue, 51±3.3mg/g dry tissue, respectively, for the 1% treated group. Tensile strength and DNA was found to increase significantly as compared to control. Hydroxyproline levels were not found to be significant.[27]
15.	Anti-fertility	Stem	Hydro-alcoholic extract	200, 400 mg/kg for 7 days	Female Wistar albino rats	-	Percentage of implantation per number of corpora leutea	Inhibition of number of implant site in uterine horns were 0, 16.66 and 66.66% for control, 200 and 400 mg/kg dose respectively. Both doses of the extract showed significant inhibition of a number of the implant site.[28]
16.	Antithrombotic	Whole plant	Ethanolic extract	200, 400 mg/kg	Wistar rats	i.v. of carrageenan (2mg/kg) into the dorsal tail vein.	Thrombosis of the tail, Bleeding time and Clotting time	The mean length of the infarcted region in the rat tail was 10.1±0.6 cm, 9.2±0.3 cm and 6.5±0.7 cm in 200, 400 mg/kg extract and heparin treated rats, respectively. Extract significantly increased the bleeding and clotting time of the animals subjected to the test. Thus, responsible for the protective effect on thrombosis.[29]
17.	Laxative	Leaves	Hydro-alcoholic extract	Pretreatment with 100, 200 and 400 mg/kg	Wistar albino rats	1ml of castor oil orally for induction of diarrhoea	Consistency and frequency of faecal matter, Purging index	The extract increased the frequency of defecation also the number of wet and deformed faeces. The extract increased the purging index to 286.22 compared to 201.63 for vehicle control. The extract produced diarrhoea which was 20.29% more than the castor oil alone.[16]

EN- *Euphorbia neriifolia* Linn., TFEN- Triterpenoid fraction of EN, CFA- Complete Freund's Adjuvant, TNFα- Tumor Necrosis Factor-alpha, ENF- EN flavonoid, DENA- N Nitrosodiethylamine, LPO- Lipid peroxidation, SOD- Superoxidase dismutase, CAT- Catalase, GST- Glutathione S-Transferase, GSH- reduced glutathione, AST- aspartate aminotransferase, ALT- alanine aminotransferase, ALP- alkaline phosphatase, TP- total protein, TC- total cholesterol, ENEE- Ethanolic extracts of *Euphorbia neriifolia* Linn., OGTT- Oral glucose tolerance test, FBG- fasting blood glucose, HDL- High-Density Lipoprotein, LDL- Low-Density Lipoprotein, VLDL- Very Low-Density Lipoprotein, TLC- Total Leucocyte Count, DLC- Differential Leucocyte Count, ENSF- Saponin Fraction of EN

DISCUSSION

This systematic update confirms that Snuhi (*Euphorbia neriifolia* Linn.) is an important plant species with a plethora of pharmacological activities. In this article, a comprehensive review of *In Vivo* Studies of pharmacological activities of Snuhi is discussed under the headings as - pharmacological activities, plant part used, type of extract, a dose of extract, the animal model used, specific investigations and findings (Table 3). A total of 17 *In Vivo* Studies on the pharmacological activities of Snuhi were screened. Among them, 3 were of anti-inflammatory activity, two each were of analgesic, anticancer, antidiabetic, antilipidemic, wound healing and hepatoprotective activities and one each were of other activities.

Plant parts used for experiments were leaves, stem, latex, and whole plant. Most studies reveal leaves as a plant part for solvent extraction.

The type of extract used was alcoholic, hydro-alcoholic, triterpenoid, hydro-ethanolic, ethanolic, petroleum ether, chloroform, acetone, saponin fraction and aqueous extract. The hydro-alcoholic extract is the mainly used extract.

Dose of extract used were 5, 10, 20, 40, 80, 100, 150, 200, 250, 400, 500, 750 mg/kg (or ml/kg) as per animal body weight. 200 and 400 mg/kg is the most common used dose for the studies.

Animal models used were Frog, Guinea pig, Wistar albino rats, Swiss albino mice, and Sprague Dawley rats. The review shows that Wistar albino rats are the most used animal models for *In Vivo* studies.

Induction of disease for pharmacological activities was done as per the activities. Carrageenan induction for paw oedema is a well-established and widely used inducer to evaluate the anti-inflammatory potential of plants and drugs. The inducer used for Anticancer activity was DENA. The study on wound healing activity reveals wound formation by excision.

Specific investigations were also done as per the activities.

Findings of the studies were found to be suggestive of proven activities.

The hydroalcoholic extract of 400 mg/kg of leaves was the most significant anti-inflammatory activity with 69.47% inhibition of oedema volume (Table 3, SN 7. i.). Very few attempts were made to study *In Vivo* anticancer activity of Snuhi. By reviewing both the studies on *In Vivo* anticancer activity, results were nearly the same via neutralising the oxidative stress induced by DENA and exerting its defensive property by regaining the expected levels of SOD, GST, CAT, GSH, SGOT, SGPT, ALP, TC, TP, creatinine, urea, Cyt P450 and Cyt b5 (Table 3, SN 5. i. and ii.). Antilipidemic studies showed a significant reduction in cholesterol. But the difference between the reduction of

cholesterol in the two studies is minute as 73.0±1.57 mg/dl and 73.23±3.16 mg/dl, respectively (Table 3. SN 8 i. and ii.).

Investigations used to prove the activity were nearly the same in wound healing activities. Still, the routes of administration of extract were different, i.e., oral and local application (Table 3. SN 14. i. and ii.). Hepatoprotective studies divulge ENSF extract decreased SGOT, SGPT and ALP levels against Carbon tetrachloride-induced liver damage in rats (Table 3. SN 13. i.). However, the subacute effect of Ethanolic extracts treatment decreased serum SGOT with no effect on SGPT. Also, it showed an extremely significant rise in liver SOD and liver catalase and reduced liver peroxidation (Table 3. SN 13. ii.).

Investigations used to prove Analgesic activities were the tail-flick method and Eddy's hot plate method (Table 3. SN 2. i.), whereas Thermal stimulus, Mechanical stimulus and Chemical stimulus for another one. (Table 3. SN 2. ii.)

CONCLUSION

Present analysis accomplishes *In Vivo* pharmacological activities of Snuhi (*Euphorbia neriifolia* Linn.), i.e., anaesthetic, analgesic, anti-anxiety, anticonvulsant, antipsychotic, anti-arthritis, anticancer, antidiabetic, anti-inflammatory, antilipidemic, antioxidant, antiulcer, diuretic activity, immunomodulatory, hepatoprotective, wound healing property, anti-fertility, antithrombotic and laxative activities. The scientific data on *In Vivo* studies of Snuhi compiled in this review article will be helpful to researchers for further studies. More thorough *In Vivo* studies are needed to ascertain the efficacy and acute toxicity of Snuhi and its formulations. Also, there is a need to conduct clinical research further to validate Snuhi and its formulations for pharmacological activities.

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Cite this article as:

Sayli W. Wadhai *et al*. *In Vivo* pharmacological activities of upavisha snuhi (*Euphorbia neriifolia* Linn.): A review. Int. J. Res. Ayurveda Pharm. 2022;13(3):79-85 http://dx.doi.org/10.7897/2277-4343.130364

Source of support: Nil, Conflict of interest: None Declared