An Elucidated Study on Action of alkaloids and Pathophysiology of Rananculaceae Family with Special focus on Genus Pulsatilla

Dr.Sheetal.A.P.*[1], Dr Tejaswini.K. *[2] Dr. Sai.B *[3]

Bharati Vidyapeeth (Deemed To Be University) Homoeopathic Medical College, Dept. Of Post Graduate &Research Centre, Pune-Satara Road, Katraj, Dhankawadi, Pune, India - 411043

Department Of Homoeopathic Materia Medica.

Corresponding Author Details:

***1 Dr.Sheetal Ajit Patil M. D(HOM)**

Designation: Associate Professor of Department of Homoeopathic Materia Medica.

Present Address: Bharati Vidyapeeth (Deemed To Be University) Homoeopathic Medical College, Dept. Of Post Graduate &Research Centre, Pune-Satara Road, Katraj, Dhankawadi, Pune, India - 411043.

Contact No – 9850545835

Email – sheetal.patil@bharatividyapeeth.edu

[2] Dr. Tejaswini Khachane

Designation: P.G. Scholar of Homoeopathic Materia Medica.

[3] Dr. Perla Sai Bhuvaneshwari

Designation: P.G. Scholar of Homoeopathic Materia Medica.

Abstract :

Background: In this present study, the alkaloids of Genus Pulsatilla from Rananculaceae are studied. Genus Pulsatilla has different alkaloids they are anemoin,protoanemonin, tannin, flavonoids, triterpenoid saponin and rananculin.This alkaloids are obtained by HPLC fractionation and they are proved in in-vitro and in-vivo study.Every alkaloid have its own activity or properties. Genus Pulsatilla has different properties like anti-tumor, anti-cancer, anti-oxidant, anti-infammatory, anti-bacterial, anti-viral. It is useful wile treating diabetes, dysentry, dyspepsia, coryza, rhinitis, otitis, uterine tract infection (UTI) and many others.

Materials & Methodology: The above mentioned are taken from different databases like Google, Google scholar, Pub-Med and Research Gate. This article is about the action of alkaloids of Pulsatilla which helps to know its clinical use. Its physiology of alkaloids on body.

Keywords: Pulsatilla, Alkaloids, Properties, Traditional uses, Phytoconstituents, Clinicals Condition.

DOI Number: 10.48047/nq.2022.20.19.NQ99240 **NeuroQuantology2022;20(19): 2828-2834**

1.Introduction:

Rananculaceae family also known as buttercup family. Asia indicated that only one-third of the ranunculaceous genera are common to both areas i. e. Caltha, Trollius, Actaea, Cimicifuga, Aconitum, Delphinium, Aquilegia, Anemone, Pulsatilla, Adonis,

Thalictrum, Ranunculus, all of them are shared with the flora of the Circumboreal Region. In India, 6 genera and 10 species found and all are concentrated in the high mountain flora of the Deccan Plateau, West and East Gaty ridges.[1]

Genus Pulsatilla comprises 70 species, most are grown in Turkey, Russia, Germany,France,Asia, Southern England, Sweden, and Demnark.Pulsatilla is a sister to Anaemone. Most plants grow in dry, sun-exposed regions like subalpine and alpine regions, dry heathlands, etc.[2,,5] Main species of genus Pulsatilla are Pulsatilla chinensis,pulsatilla nigricans, Pulsatilla Patens, Pulsatilla Alba, Pulsatilla pratensis,.[3]

1.1Morphology:

Pulsatilla is also known as wind flower,its a kind of pernnial herb. The Pulsatilla nigricans has a stem that is simple, erect, rounded, and between three and five inches high. The leaves are radical, pinnatifid, downy, with many-parted segments that have linear lobes. The flowers are solitary, terminal, pendulous, deep purple or violet-brown, with six sepals and stalked glands or sterile stamens between the fertile stamens and sepals.[3,4,5] Long, silky hairs are frequently found covering the plants of Pulsatilla species. Their solitary, bisexual flowers have three bracts who connect to form a bell-shaped involucre. The stamens are usually numerous, with the outermost ones resembling degraded petals. There are always six petals.[4]

1.2Phytoconstituents:

Glycoprotein, Pulsatillic acid, Triterpene saponins ,lignan, Anemosapogenin, Betulinic acid, Anemonin, these alkaloid are obtain in Pulsatilla Chinesis.[2]

From P turczaninovii 7 triterpenoid saponins isolated they are Pulsatilla saponin A3, pulsatilla saponin B4, 23-hydroxybetulinic acid, pulsatilloside B, pulsatilloside C, cirenshenoside S and oleanolic acid.[5]

Deoxypodophyllotoxin, which was isolated from the roots of *P koreana,* was found to inhibit the tube-like formation of HUVECs (human umbilical venous endothelial cells) and have a potent antitumor effect.[6]. In reversed phase HPLC analysis of Pulsatilla chinesis eleven triterpenoid saponins (compounds 1–11) are isolated. [3,7,25].

Nine triterpene saponins, isolated from the roots of P. chinesis (Bunge) Regel were put to the test for their ability to be cytotoxic by Mimaki et al. Pulsatilla Chinesis contain 36 triterpenoidal saponin which is subdivided into oleanolic acid glycosides, hederagenin glycosides, 23-hydroxy betulinic acid glycoside and betulinic acid glycosides [10].

A triterpenoid glycoside called patensin was discovered when the roots of Pulsatilla patens var. multifida were extracted using ethanol.[9]

In chromatographic fractionation of Pulsatilla vulgaris and Pulsatilla Patens there is isolation of two oleanane-type glycosides identified as hederagenin 3-*O*-β-d-glucopyranoside (2.7 mg) and hederagenin 3-*O*-β-d-galactopyranosyl-

(1→2)-β-d-glucopyranoside (3.3 mg, patensin)[psd].

Pulsatilla Alba contain two alkaloids which are lactone compounds anemonin ad protoanemonin.Anemonin have antipyreting effect and protoanemonin has sedating effect. Anemonin acts thorugh the mechanism which is follwed by Dopamine. Anemonin is more potent than protoanemonin.[17]

Protoanemonin is a mutagenic, reactive substance having an exocyclic methylene group. Numerous pharmacological features of pulsatilla saponin D (C47H76O17), including significant tumour growth suppression and antifungal, antibacterial, and cytotoxic actions, have been reported. Hederagenin, the active component in other species' extracts containing triterpenoid saponins, significantly inhibited the transporters for serotonin (5-HT), norepinephrine (NE), and dopamine (DA). The methanolic extract of P. Nigricans flavonoids and tannins have a strong antianxiety effect [20,22,] Ranunculin, a terpenoid glucoside that is the active component in fresh plant material, is converted to protoanemonin [23]. *Pulsatilla* genus contain ranunculin, anemonin, protoanemonin, triterpenes, and saponins (9%) of mainly the oleanane and lupane-type.[18]**.**Flavenoids and saponin are the main constituents of Pulsatilla species.[27]

1.3Traditional Uses:

Pulsatilla is use as medicine in Chinese medicine for the treatment of problems caused by bacteria like entrirtis and baciilary dysentry. It cures bacterial infection by suppressing and killing bacterial pathogen.It is effective in eliminating fever and cleaning toxic materials.It prevents and cure infectious diseases. P. nigricans is used to treat anxiety, depression, moderate restlessness, and mental disturbance (3). It has higher efficacy infectious diseases that antibiotics as it has lesser side effects, less toxicity,and less drug resistance.[6] The plant has been used as a treatment for orchitis, epididymitis, ovaritis, ovaralgia, debility-related discomfort, and pain brought on by acute inflammation. While decreasing morbid sexual excitement, it boosts sexual power. P. nigricans treats amaurosis, cataracts, corneal opacity, urethral irritation, and the resulting spermatorrhoea and prostatorrhoea. P. nigricans has been used as a taeniafuge(to expel worms) and to treat acute meningitis, dyspepsia, coryza, otitis, rhinitis, conjunctivitis, coughs, and cutaneous diseases (12). The roots of P. nigricans have been utilised in traditional Chinese medicine for their blood-cooling and detoxifying properties.The methanolic extract of Pulsatilla Nigricans (syn of Pulsatilla pratensis Mill) inhibits hyaluronidase.[26]

Pulsatiila Vulgaris used as traditional medicine in Chinese and Korean medicine in the treatment of bronchitis, cough, headaches, neuralgia, sleeplessness, hyperactivity, and bacterial skin infections.[7]

Pulsatilla Koreana has cytotoxic properties so it is used to treat various cancer.It has anti-tumor and antioangiogenic activity.[8]
Pulsatilla chinesis is used in treatment of intestinal amebiasis, malaria, vaginal trichomoniasis and bacterial infections.It has anti-inflammatory action.[9,10]

2.Methods:

A systematic review was conducted to study the alkaloids of Genus Pulsatilla in published studies to know the action and properties of Pulsatilla. This article also discuss about Pulsatilla alkaloids and their properties.

3.Study strategies:

This studies are taken with the following search strategy terms 'Pulsatilla', 'Pulsatilla alkaloids', 'Pulsatilla chemical constituents', 'Pulastilla nigricans', 'Pulsatilla chinesis, 'Pulsatilla Alba',Triterpenoid saponin', protoanemonin, The above mentioned are taken from different databases like Google, Google scholar, Pub-Med and Research Gate.

4.DISCUSSION:

Ranunculin inhibits DNA polymerase, causi ng it to be toxic to KB cells. The majority of t he large intestine's facultative anaerobic ba cterial population belongs to this strain. It is challenging to treat since it is resistant to a ntimicrobial drugs and can result in diarrho ea, intestinal disorders, sepsis, meningitis, a nd inflammation of the urinary tract. In in-vitro cytotoxic study of triterpenoid saponin isolated from Pulsatilla Chinesis studied against HL-60 cells.It exhibited excellent cytotoxicity against HL-60 cells.[7]

In Pulsatilla koreana root along with 11 known saponins, six saponins, five lupanes (1–5), and one oleanane were isolated. All extracted substances were tested for their cytotoxic effects on
A-549 human lung carcinoma cells, which showed anti-angiogenic properties and effective anticancer properties in mice harbouring Lewis lung carcinoma.Triterpenoid Saponin has anti-tumour, anti-inflammatory,anti- fungal, anti-HIV.[10]
Pulsatilla chinensis, pulsatillic acid, 23 hydroxybetulinic acid, and three new lupane type triterpene glycosides, namely pulsatillosides A, B, and C, were isolated from plants that grow in China. Two new and several known oleanane type glycosides and two known lignanes were isolated from plants that grow in Japan1. P. chinensis root methanol extract contains a glycoside component that has cytotoxic properties toward human leukaemia HL60 cells.[8]
Flavonoids possess antioxidant, Hepatoprotective, antibacterial, antiviral, anti-cancer activity.It is used in severe degenerative diseases related with cardiovascular diseases,cataracts,cognitive dysfunction and cancer.[13,14]
Diseases including cancer, cardiovascular disease, diabetes, and asthma are largely influenced by inflammation as flavonoids have anti-inflammatory property its useful in treating this diseases.[15]
In in-vitro study of Protoanemonin it is tested that it has anti-fungal action against the yeast form of Candida albicans.[16]

Anemonin and Protoanemonin has anti-pyretic and sedating property respectively. Protoanemonin has a action against Protoanemonin has activity against Gram-positive and Gram-negative bacteria, yeast, and fungi.

In vitro and in vivo study of Pulsatilla chinesis shows anti-tumor activity against malignant tumor and cytotoxic activity against three cancer cell lines (A-549, human lung cancer; SK-MEL-2, human melanoma, MCF-7, human breast cancer). [21,22]

Protoanemonin is an irritating lactone that r esults in allergic dermatitis on human skin, as well as gastrointestinal distress and centr al nervous system paralysis internally. It has previously been claimed that protonaemon in has antifungal and antibacterial activities. [24]

5.ACKNOWLEDGEMENT:

Many thanks go to the Almighty who helped me and filled me with all postivity to go ahead in all circumstances.I would like to express my gratitude and appreciation to all those who gave me the possibility to complete this report. I take this oppurtunity to experss my deep sense of gratitude to the Head of the Department of Homoeopathic Materia medica Prof.Dr.Vaishali.V.DolasM.D.(Hom) who supported at all times and never let me down.

I would also like to extend my thaks to the P.G.CoOrdinator Prof. Dr.Anitha.Patil M.D(Hom), Ph.D who helped me all time. It gives a great pleasure to have this opurtunity to express my thaks to THE PRINCIPAL Prof. Dr.AVINASH.R.MEHTRE, M.D.(Hom) for giving this oppurtunity. Last but not least I would like to thank Honorable Dr.Samuel Hahnemann for Discovering these Great Homoeopathic Laws and giving us new oppurtunity to serve the Humanity.

References:

1.Ziman, S. N., & Keener, C. S. (1989). A Geographical Analysis of the Family Ranunculaceae. *Annals of the Missouri Botanical Garden*, *76*(4), 1012–1049. https://doi.org/10.2307/2399690

2. Kumar S, Madaan R, Farooq A, Sharma A. The genus Pulsatilla: A review. Pharmacognosy Reviews. 2008;2(3):116.

3. Strzałkowska-Abramek M, Jachuła J, Dmitruk M, Pogroszewska E. Flowering phenology and pollen production of three early spring Pulsatilla species. Acta Scientiarum Polonorum. Hortorum Cultus. 2016 Jan 1;15(6):333-46.

4. Li QJ, Wang X, Wang JR, Su N, Zhang L, Ma YP, Chang ZY, Zhao L, Potter D. Efficient identification of Pulsatilla (Ranunculaceae) using DNA barcodes and micro-morphological characters. Frontiers in plant science. 2019 Oct 9;10:1196.

5. Goyal S, Chawla R, Kumar S. Recent advances and sporadic phytochemical and pharmacological review on potential herbs of the genus “Pulsatilla”. Pharma Science Monitor. 2017;8(3):375-409.

6. Hu Y, Chen X, Duan H, Hu Y, Mu X. Pulsatilla decoction and its active ingredients inhibit secretion of NO, ET-1, TNF-α, and IL-1α in LPS-induced rat intestinal microvascular endothelial cells. Cell Biochemistry and Function: Cellular biochemistry and its modulation by active agents or disease. 2009 Jul;27(5):284-8.

7. Łaska G, Sienkiewicz A. Antifungal activity of the rhizome extracts of Pulsatilla vulgaris against Candida glabrata. European Journal of Biological Research. 2019 May 25;9(2):93-1030.

8. Bang SC, Kim Y, Lee JH, Ahn BZ. Triterpenoid saponins from the roots of Pulsatilla koreana. J Nat Prod. 2005 Feb;68(2):268-72. doi: 10.1021/np049813h. PMID: 15730260.

9. Glebko LI, Krasovskaj NP, Strigina LI, Ulanova KP, Denisenko VA, Dmitrenok PS. Triterpene glycosides from Pulsatilla chinensis. Russian chemical bulletin. 2002 Oct;51(10):1945-50.

10. Xu K, Shu Z, Xu QM, Liu YL, Li XR, Wang YL, Yang SL. Cytotoxic activity of Pulsatilla chinensis saponins and their structure–activity relationship. Journal of Asian natural products research. 2013 Jun 1;15(6):680-6.

11. Pietta PG. Flavonoids as antioxidants. Journal of natural products. 2000 Jul 28;63(7):1035-42.

12. Kumar S, Pandey AK. Chemistry and biological activities of flavonoids: an overview. The scientific world journal. 2013 Oct;2013.

13. McClure JW. Physiology and functions of flavonoids. InThe flavonoids 1975 (pp. 970-1055). Springer, Boston, MA.

14. Maleki SJ, Crespo JF, Cabanillas B. Anti-inflammatory effects of flavonoids. Food chemistry. 2019 Nov 30;299:125124.

15. Martín ML, San Román L, Domínguez A. In vitro activity of protoanemonin, an antifungal agent. Planta Medica. 1990 Feb;56(01):66-9.

16 Martin ML, Ortiz de Urbina AV, Montero MJ, Carron R, San Roman L. Pharmacologic effects of lactones isolated from pulsatilla alpin a subsp. aphfolia. Journal of ethnopharmacology. 1988 Dec 1;24(2-3):185-91.

17. Kim Y, Bang SC, Lee JH, Ahn BZ. Pulsatilla saponin D: The antitumor principle fromPulsatilla koreana. Archives of pharmacal research. 2004 Sep;27(9):915-8.

20. Martin ML, Moran A, San Roman L. Pharmacological screening of Pulsatilla alpina subsp. apiifolia. Journal of ethnopharmacology. 1987 Nov 1;21(2):201-6.

21. Xu QM, Shu Z, He WJ, Chen LY, Yang SL, Yang G, Liu YL, Li XR. Antitumor activity of Pulsatilla chinensis (Bunge) Regel saponins in human liver tumor 7402 cells in vitro and in vivo. Phytomedicine. 2012 Feb 15;19(3-4):293-300.

22. Jürgens A, Dötterl S. Chemical composition of anther volatiles in Ranunculaceae: genera-specific profiles in Anemone, Aquilegia, Caltha, Pulsatilla, Ranunculus, and Trollius species. American Journal of Botany. 2004 Dec;91(12):1969-80.

24. Hao DC, Gu X, Xiao P. Anemone medicinal plants: ethnopharmacology, phytochemistry and biology. Acta pharmaceutica sinica B. 2017 Mar 1;7(2):146-58.

25 Ye WC, Ji NN, Zhao SX, Liu JH, Ye T, McKervey MA, Stevenson P. Triterpenoids from Pulsatilla chinensis. Phytochemistry. 1996 Jun 1;42(3):799-802.

26 Singha H, Dasgupta RK. ANTI-HYALURONIDASES ACTIVITY OF CRUDE EXTRACTS OF PULSATILLA NIGRICANS.

27. Cushnie TT, Lamb AJ. Antimicrobial activity of flavonoids. International journal of antimicrobial agents. 2005 Nov 1;26(5):343-56.

7.Liu Q, Wang P, Zhang L, Guo T, Lv G, Li Y. Concise synthesis of two natural triterpenoid saponins, oleanolic acid derivatives isolated from the roots of Pulsatilla chinensis. Carbohydrate research. 2009 Jul 27;344(11):1276-81.