Review on Medicinal plant Phyllanthus Niruri and its Effects

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Abstract: This review article focuses on the widely used Phyllanthus Niruri, which is also called as 'keezhanelli' in Tamil and belongs to the group of family called "Euphorbiaceae", which is specially grown in regions of 'India, Sri Lanka, Indonesia, and other tropical areas'. The leaves of the medicinal plant are used substantially in Ayurveda and native medicine to cure various diseases such as 'liver damage, hepatitis, jaundice, renal disorders, enteritis, diarrhoea, and dropsy'. It discusses the wide variety of phytochemical properties, pharmacological properties, anti-malarial reactions, anti-cancer reactions, anti-platelet reactions, and antimicrobial reactions. The parts of those plants have many active phytochemicals.

Keywords: Phytochemical, Anti-Malarial, Pharmacological, Anti-Microbial, Anti-cancer, Anti-platelet, Therapeutic property.

1. INTRODUCTION

The Phyllanthus Niruri is also known as 'Keezhanelli' in Tamil and belongs to the family of Euphorbiaceae. (16) It is specially grown in regions of India, Sri Lanka, Indochina, etc. (15) At the tropic of centre Phyllanthus belongs to the taxonomy of genus which includes lots of herbs, shrubs, and trees, and consists of more than 600 species, including "P. amarus, P. patches, and P. neurons. P. anisolobus, P. Emblica, and P. Oxyphyllus" were explored for their phytochemical and pharmacological properties. (8) Phyllanthus Niruri often called 'chamber better, gripe weed, shatter stone' is a herb. (11) Species of suffruticose in the pharmacopeia of Bin PR of China in the plant Phyllanthus area, which is called as "Ye Xia Zhu". (7) On the basis of Phyllanthus species, Phyllanthus Niruri is a little, tall, perennial herb native to the Amazon rain forests and other tropical regions that can attain heights of up to forty cm. Its leaves are 1 to 12cm long and there is alternate sensible oblong. It has small off-white greenish flower. A typical plant of the phyllanthaceae genus with significant ayurvedic, Chinese, and Malay ethnomedical histories is Phyllanthus Niruri. Phyllanthus Niruri have been attributed to geranium and confirmed by its cholesterol and triglyceride lowering effects. It is used in Indian ayurvedic system for ancient time. It is having very short life. It is bitter in taste but sweet in post digestive effect and is also used as astringent. Pharmaceuticals made from plants may be acquired easily, tend to be less pricey, secure, and efficient, and they rarely trigger side effects. The herb Phyllanthus Niruri, additionally referred to as "dukonganak" locally, is small. Many of these are used in modern health care as active ingredients or as precursors in searching for new medicinal products.



Fig 1. Phyllanthus Niuri leaves



Fig 2 Phyllanthus Niruri flower and fruit.

2. ANTIMICROBIAL ACTIVITY

Phyllanthus Niruri is a member of the 'Euphorbiaceae family' and offers several health advantages, one of which is antibacterial activity. (5) The anti-microbial agents in vitro, in vivo and human studies have all been conducted. It was discovered in rabbit in vivo investigations. (8) Increased WBC and neutrophil concentrations, reduced haemoglobin and Escherichia coli-infected lymph cells,, although while provided, the level of enzymes remains unchanged. (1) Phyllanthus Niruri as a dosage to overcome antibacterial resistance Rabbit activities Lactobacillus bacteria were grown in vitro. (6) They discovered curd was taken and researched even there by introducing the microbial activity has been lowered. (5) This plant in clinical studies with hepatitis B virus infection patients, fifty percent to sixty percent of those who received Niruri, P. were shown to respond. HBsAgsero conversion occurred in the extract. (8) The decrease in HBsAg antigen might be attributed to P. niruri's inhibitory effect on hepatitis B viral genetics. (7) In an investigation, sufferers received therapy using components from all three Phyllanthus species. It was found that the niruri plant extracts functioned superior. (13) Although more likely to cause decreases in HBeAgtiters, not all of the bio agents responsible for antihepatitis protection are P. niruri activity has been detected, and molecular analyses have been conducted. (5) They have figured out the molecular structure of new lignin.

3. ANTIBACTERIAL ACTIVITY:

3.1. Preparation for Antibacterial and Antifungal Activity Of Disc

Using sterile Whatman, prepare the disc for antibacterial and antifungal activity. A 5mm diameter disc of No. 1 fitter paper was created. 20 ml of extracts from Phyllanthus Niruri in four different concentrations—2mg/ml, 4 mg/ml, 6 mg/ml, and 8 mg/ml—to vary the antibacterial and antifungal activities. (18)

3.2. Collection of Microbial Culture

Bacillus subtilis, Escherichia coli, and Aspergillus Niger are fungal cultures that can be found in the collection of microbial cultures from the botany and microbiology departments.

Determination of Antibacterial activity of Phyllanthus Niruri:

3.3. Preparation of Bacterial Inoculum

Making a bacterial inoculum to test Phyllanthus Niruri's antibacterial activity. It was made by adding a loopful of test organisms to 5 m of nutritional broth and incubating it at 37 °C for 3–5 hours until moderate turbidity occurred.

3.4. Disc Diffusion Method

By using the dissolution method, a methanol plant extract of P-antibacterial niruri's activity was created. Twenty millilitres of nutrient agar were imposed in Petri dishes to grow and allowed to become established. On the surface of the agar, 1 mL of the inoculum that was previously created was poured and evenly disseminated. Excess inoculum is drained away. Once the disc had dried, the extracts were applied to the plates' surfaces with sterile forceps and gently pressed to ensure contact with the agar. For 24 hours, the plates were incubated at 37°C. The millimetre-scale Zone of Inhibition was measured and observed. Granzyme expression of Zach, a patient with anorectal cancer, before and after taking Phyllanthus Niruri Sinn (PNC).

3.5. Study Procedure

Every patient who participated in this study had a colonoscopy biopsy. Following a colonic biopsy, the patients received treatment with Dal 100 mg PNL Extract Stimuno R daily for 14 days. After 14 days of therapy, the tumour was removed. Granzyme tumour cell expression was quantified by immune histochemical labelling. The microscopic diagnosis and immune histochemical staining were carried out, etc.

3.6. Statistical Evaluations

The average, standard deviation, (SD), and midpoint were employed to show information regarding the ratio of Granzyme. With the support of SSPS ver-18-0 for Windows, statistical investigation was conducted with the price established at £006.

4. ANTICANCER ACTIVITY

4.1. Materials & Methods

4.1.1. Ethical Approval

This project has received approval from the 'Dr. Kariadi General Hospital Ethical Clearance Committee' at "Diponegoro University in Semarang", Indonesia. All patients' consent was received from Stratton for the study. (20)

4.1.1. Study Setting and Patients

Granzyme expression was tested as a measure of cancer cell growth inhibition following the administration of PNL with one group of patients who had colorectal carcinoma in an earlier and post-study approach. From May - July 2016, the Dr. Kariadi general hospital in Semarang, Indonesia, was the site of the study. (21)

- Zach's anorectal tumor patients granzyme activity prior to and following receiving Phyllanthus Niruri Sinn (PNC) treatment. (21)
- Expression of granzymes (%), median (Min-Max)

Table 1. Expression of granzymes			
PATIENT ID	PRE-TREATMENT	POST-TREATMENT	
A	24.93(15.31-30.45)	59.65(37.55-81.63)	
В	20.03(13.79-33.16)	49.75(37.08-65.64)	
С	26.28(15.19-53.50)	70.77(54.92-83.72)	
D	16.60(10.21-23.56)	70.69(60.00-81.43)	
E	29.73(13.06-49.13)	67.62(37.61-88.11)	
F	21.49(9.46-28.00)	68.96(60.90-86.23)	
G	20.33(15.65-31.90)	80.09(71.11-86.09)	
Н	23.61(17.79-28.57)	69.16(55.67-86.52)	
1	34.36(17.43-51.69)	70.71(55.05-84.09)	
J	29.94(14.00-49.43)	68.14(38.68-88.65)	
К	24.44(18.64-31.68)	71.29(55.21-83.95)	
L	29.38(12.63-48.84)	67.29(37.16-87.98)	
M	15.66(32.84-42.70)	60.29(39.80-76.26)	
N	25.56(18.69-34.84)	53.93(39.59-70.60)	
0	23.95(15.32-29.41)	57.37(46.61-70.39)	
MEDIAN	24.93(16.60-34.36)	68.15(49.75-80.09)	

Findings this study add to the mounting evidence from earlier investigations that PNL has promising anticancer properties. According to a study, PNL extract exhibited anticancer properties and could stop hepatic carcinoma cell lines. According to a study, spray-dried PNL extract promoted apoptosis and reduced liver cancer cells' lifespan. (20) Specifically for colorectal cancer, a Wistar rat study was demonstrated that PNL prevented colorectal cancer from developing, greatly it reduced tumour development and cancer cell survival. (32) AgNORs are a proliferation indicator of cancer cells. The dose of mixed spray-dried PNL extract is demonstrated a noticeably stronger cytotoxic impact when combined with cisplatin. The outcomes of this research indicate that PNL may be useful as a gastrointestinal chemotherapy and as a drug against cancer. This experiment only involved one group and had no positive results. (20)

5. ANTI-PLATELET ACTIVITY

Damage to blood vessels during the early stages of thrombosis generates the creation of sticky proteins and soluble agonists near the injury site. This triggers platelet activation. Adhesion, activation, and aggregation, all of which culminate in the creation of thrombus rich in platelets (Jackson et al., 2003). (34) Activated Platelets help thrombin production by acting as catalysts the area where coagulation activation can take place. Thrombin not only contributes to the synthesis of fibrin but also functions. (30) A powerful platelet activator the expanding assemblage of Cross-linked fibrin finally stabilizes active platelets. This causes the development of a platelet-rich thrombus (Ross 1993). (14) Platelet aggregation (PA) increased as a result of increasing In vivo platelet sensitivity to agonists leading to the beginning of the advancement of atherosclerosis and the incidence. The production of blood platelets is currently undergoing equilibrium. Blood loss is accurately controlled by contacts between the vessel wall's components, blood's circulating platelets, and the system's normal homeostasis. (33) The adhesion of platelets to blood vessels and their combination to release a bio-reactive substance increased the levels of atrial thrombosis and atherogenesis, are the causes of life-threatening illnesses such as unstable angina, myocardial infarction, and

reclusion after angioplasty. Inhibiting platelet aggregation is important for the prevention and treatment of heartrelated disorders. Aspirin performs exceptionally well in the process of inhibiting platelet activity. (34).

5.1 Materials and Methods

5.1.1. Determination of PT

5.1.2. Principle

The optimal concentration of thromboplastin and calcium is incubated with plasma to start the coagulation process. The time it takes for a fibrin clot to develop is then determined. (14)

5.1.3. Reagent Used

Fresh standard human plasma, PT Reagent, and sodium citrate solution are used to measure reaction time. (15).

5.1.4. Procedure

Carefully mixing 1 part of sodium citrate (0.11 mol) with 9 parts of venous blood prevented foam from forming. The blood sample was centrifuged at 1500 p.m. for 15 minutes at room temperature and it was then stored in a sealed tube for no more than 5 minutes. After blood collection, the plasma was examined within 24 hours. (34)

5.2 Determination of APT

5.2.1 Principle

Heparin presence and the absence of one or more intrinsic pathway clotting factors are both indicators of APTT of plasma. The amount of time needed for a clot to develop is measured and used to assess the plasma's anticoagulant status. (15)

5.2.2. Reagent Used

- *APTT Reagent
- *Calcium chloride
- *TSC solution.

5.2.3. Procedure

Fresh plasma was used throughout the test since it was effective at the time of the test. as soon as possible as opposed to storing plasma. To prevent foam formation, an anticoagulant was added right after 9 parts of whole blood from veins were placed into a clean test tube with 1 part of TSC Solution. It was spun at 8000 rpm for 15 minutes to separate the test tubes to collect the plasma. (30).

6. ANTI-PLASMODIUM ACTIVITY

Plasmodium is the genus that contains the protozoa that cause the contagious disease malaria. Malaria continues to be an important public health concern in Nigeria, as 76% of people is at peril. Many medications have their roots in medicinal plants like quinine and artemisinin. (4)

Plant extracts have been evaluated in human studies for use in the management of elevated blood pressure, yellowing of the skin type 2 diabetes, hypercalciuria, and urinary stone formation. P. Amarus plant has numerous 440

ethnobotanical applications, including parasites, diarrhoea, dysentery, and inflammation. Alkaloids, flavonoids, and hydrolysable tannins of organic compounds of medicinal plants of different classes are from P. amarus. P. Amarus' anti-plasmodial activity towards the parasite P. Falciparum has been evaluated in vitro, along with the acute damage profile. (16)

6.1. Materials and Methods

i) Blood Sample collection for in vitro assay

The study included with the affected one who require testing for diagnosis have been referred to the laboratories segment. testing between August 1 and November 30, 2019.P. falciparum infection screenings were conducted on patients who were not receiving antimalarial medication. (17)

ii) Extraction solutions and culture medium production:

Dissolve 960 ml of distilled water and 0.5 ml of gentamicin in a biosafety cabinet, sterilize it with 0.45 and 0.22 membrane fitters, and then store it there at 4 °C until you need it. To keep the pH of the medium constant before cultivation, it was added with sodium bicarbonate and 5% albumin (19).

iii) Experimental animal:

They use adult albino rats. Before use, those animals had a seven-day adaptation session at the ambient temperature. They were kept in standard enclosures and fed on standard animal's particles and fluid.

The most prevalent species, which are employed in particular regions of India, are effective for the treatment of specific illnesses such as digestive tract, genitourinary, breathing, and dermatological disorders. P. Niruri extracts take over numerous biological activities which include cardio protective, antihypertensive, antioxidant, and antiplasmodial effects. Some parts of P.niruri's activities were reported recently such as anti-tumour, anti-inflammatory, and anti-microbial from P niruri Extract. The height of the herb is 30–40 cm. (26)

The length of the leaves is assumed to be 18–14 cm in alternate and sessile structure. It has small red-coloured fruits and also contains greenish-white flowers.

7. MATERIALS OF METHODS

7.1. Collection of plant Materials

The University of Agriculture's environment was used to collect P. niruri plants from Michael Opera's environment. The plants were rinsed carefully in clean water to eliminate any earthy materials, and then they were spread out on a clean surface to air dry. (16)

7.2. Text for the potency of organism:

The bacteria that were employed in the research came from a stock culture at a federal medical facility. The vitality of each isolate was tested by reviving the organisms in nutrient agar plants. (17)

7.3. Confirmation for test organisms:

Bacterial isolates that were obtained from stock cultures have been confirmed. The Cream Stain method and a specific biochemical test were used.

8. ANTIBACTERIAL ACTIVITY EFFECT

In the past, people used herbs to treat diseases. The creation of modern pharmaceuticals for human health has continued to be based on plants for several years. They are extremely valuable and crucial for medicinal plants. The use of numerous human diseases in treatment Pharmaceuticals use plants mostly as first-isolated from plants and then used in drug manufacturing. (19) Agriculture, cosmetics, and perfumery are also used in pharmaceuticals. Ginseng has been identified from several Phyllanthus Niruri parts. It has been proven that the extracts found in herbs have a variety of medicinal effects. (26) Thus, this study summarises the various structural aspects of phytochemicals, as well as their pharmacological characteristics and impacts, including anti-cancer capabilities, among others. Additionally, it is used for research studies found to include a variety of saponins and sapogenins. (16) In another technique, aspirin is a chemical duplicate of the active analgesic chemical present in willow tree bark. Digoxin is one of the main components of several treatments for heart problems. The extracts include flavonoids, alkaloids, terpenoids, lignans, polyphenols, tannins, coumarins, and saponins, among others. (17)

CONCLUSION

According to scientific research, P. niruri has the potential to be used as a medication in the treatment of viral infections and liver diseases. (26) Despite this, the large range of research studies and inconsistent reporting requirements make it difficult to compare studies meaningfully and to conceal the capacity to reproduce these findings. As a result, results are carefully analysed, and best practices should be used in all future research. (20) Additional toxicological, mechanistic, and productivity-boosting studies would support the expansion of clinical trial investigations. Several phyllanthus including 126 terpenes, 102 phenylpropanoids, 73 phenolic compounds, 54 flavonoids, 53 polyphenols, 33 camp sterol, 31 opioids, and numerous other chemicals.(2)To evaluate their wide range of biological activities, including their anti-virus, antioxidant, hypoglycaemic, chemotherapeutic, anti-inflammatory, hypocholesterolaemia, immune modulatory, and depressive capabilities, polar solvent extracts are utilized.(4)The high amounts of phenols, flavonoids, and tannins that are thought to be found in these extracts may all have different degrees of antioxidant properties because of their hydroxide ion [340] moieties. (19) Phyllanthus methoxy's components may therefore be responsible for the majority of its bioactivities.

REFERENCES:

- [1] Asare GA, Addo P, Bugyei K, Gyan B, Adjei S, Otu-Nyarko LS, Wiredu EK, Nyarko A. Acute toxicity studies of aqueous leaf extract of Phyllanthus Niruri. Interdisciplinary toxicology. 2011 Dec;4(4):206.
- [2] Adebisi JA, Okunloye NA, Togun VA, Okwusidi JI. Phytochemical Screening, Proximate and Mineral Compositional Analyses of Phyllanthus Niruri Leaves. International Journal of Public Health, Pharmacy and Pharmacology Vol. 2021;6:1-0.
- [3] Du G, Xiao M, Yu S, Wang M, Xie Y, Sang S. Phyllanthus urinaria: a potential phytopharmacological source of natural medicine. International Journal of Clinical and Experimental Medicine. 2018 Jan 1;11(7):6509-20.
- [4] Ajala TO, Igwilo CI, Oreagba IA, Odeku OA. The antiplasmodial effect of the extracts and formulated capsules of Phyllanthus amarus on Plasmodium yoelii infection in mice. Asian Pacific journal of tropical medicine. 2011 Apr 1;4(4):283-7.
- [5] Kurhekar JV, Bodhankar MG. Antimicrobial activity of Phyllanthus niruri. Indian Journal of Natural Products. 2009;25(2):25-7.
- [6] Bagalkotkar G, Sagineedu SR, Saad MS, Stanslas J. Phytochemicals from Phyllanthus niruri Linn. and their pharmacological properties: a review. Journal of pharmacy and pharmacology. 2006 Dec;58(12):1559-70.
- [7] Bharati D, Rawat S, Sharma P. Evaluation of in vivo efficacy of aqueous leaf extract of Phyllanthus niruri in diabetic hypertensive rats. Ann ClinExp Hypertension. 2015:3:1031-7.
- [8] Shah RA, Khan S, Sonawane PD, Rehman W. Phytochemical finger printing and antimicrobial activity of Phyllanthus niruri. International Journal of Pharmaceutical Sciences Review and Research. 2017 Jun;44(2):7-11.
- [9] Venkatesh S, Reddy BM, Viswanath CK, Ramesh M. Spectrophotometric determination of hepatoprotective principle of Phyllanthus niruri Linn. Indian journal of pharmaceutical sciences. 2004;66(3):336.
- [10] Mathangi S, Deivanai MG. A Study on Development of Spice Flavoured Herb (Phyllanthus Niruri) Tea for Healthy Immune System. IJSTE-International Journal of Science Technology & Engineering. 2016;3(5):69-72.
- [11] Wongnawa M, Kaewmeesri P, Sriwiriyajan S, Mahatthanatrakul W, Ridtitid W. Effect of Phyllanthus amarus extract on the pharmacokinetics of midazolam in rabbits. Songklanakarin Journal of Science & Technology. 2014 Sep 1;36(5).
- [12] Puspita NA. Isolation and characterisation of medicinal compounds from Phyllanthus Niruri L. University of Salford (United Kingdom); 2015.

- [13] Sunitha J, Krishna S, Ananthalakshmi R, Jeeva JS, Girija AS, Jeddy N. Antimicrobial effect of leaves of Phyllanthus niruri and Solanumnigrum on caries causing bacteria: an in vitro study. Journal of clinical and diagnostic research: JCDR. 2017 Jun;11(6): KC01.
- [14] Kamal R, Mathur M, Sharma J. Antiplatelet activity of Phyllanthus nirurilinn. Elixir Appl. Biology 2012. (47): 8778. 2012 May 18;8781.
- [15] Narendra K, Swathi J, Sowjanya KM, Satya AK. Phyllanthus niruri: a review on its ethno botanical, phytochemical and pharmacological profile. Journal of Pharmacy Research. 2012 Sep;5(9):4681-91.
- [16] Ajala TO, Igwilo CI, Oreagba IA, Odeku OA. The antiplasmodial effect of the extracts and formulated capsules of Phyllanthus amarus on Plasmodium yoelii infection in mice. Asian Pacific journal of tropical medicine. 2011 Apr 1;4(4):283-7.
- [17] Aliyu K, Mohammed Y, Abdullahi IN, Umar AA, Bashir F, Sani MN, Kabuga AI, Adamu AM, Akande AO. In vitro antiplasmodial activity of Phyllanthus amarus against Plasmodium falciparum and evaluation of its acute toxicity effect in mouse model. Tropical Parasitology. 2021 Jan;11(1):31.
- [18] Ekwenye UN, Njoku NU. Antibacterial effect of Phyllanthus niruri (ChancaPiedra) on three enteropathogens in man. International Journal of Molecular Medicine and Advance Sciences. 2006;2(2):184-9.
- [19] Mwangu-Kabi ON, Nakweti RK, NdikuSL. Antiplasmodial and Antioxidant Activities of Phyllanthus Species and Associated Medicinal Plants from Kenge in the Democratic Republic of Congo (DRC). European Journal of Biology and Biotechnology. 2020 Dec 28;1(6).
- [20] Sayuti M, Riwanto I, Boediono BP, Akbar TI. Anticancer Activity of Phyllanthus Niruri Linn Extract in Colorectal Cancer Patients: A phase II Clinical Trial. Studies. 2020 Oct 1:10:17.
- [21] Sharma K, Malviya R, Gupta V. Chemo protective activity of Phyllanthus niruri and Opuntiaficusindica plant extract. Journal of Drug Delivery and Therapeutics. 2022 May 20;12(3):116-23.
- [21] Adams MR, Kinlay S, Blake GJ, Orford JL, Ganz P and Selwyn AP 2000. Atherogenic lipids and endothelial dysfunction: mechanisms in the genesis of ischemic syndromes. Annu. Rev. Med. 51:149-167.
- [22] Bounameaux H 2009. The novel anticoagulants: entering a new era. Swiss. Med. Wkly. 139: 60-64
- [23] Cai H and Harrison DG 2000. Endothelial dysfunction in cardiovascular diseases: the role of oxidant stress. Circ. Res. 87:840-844
- [24] Chopra RN, Nayar SL and Chopra IC (1986). Glossary of Indian Medicinal Plants, CSIR, New Delhi Catholic Press, Ranchi, India
- [25] Cimanga RK, Tonal, Luyindula N, Mesia K, Lusakibanza M, Musuamba CT, Apers S, De Bruyne T, Van Miert S, Hermans N, Totté J, Pieters L and Vlietinck AJ (2004). *In vitro* antiplasmodial activity of callus culture extracts and fractions from fresh apical stems of *Phyllanthusniruri*L. (Euphorbiaceae): Part 2. J. Ethnopharmacol. 95(2-3): 399-404.
- [26] Freedman JE and Keaney JF Jr. 1999. Nitric oxide and superoxide detection in human platelets. Methods Enzymol. 301:61-70.
- [27] Girach RD, Siddioui PA and Khan SA 1994. Traditional plant remedies among the Kondh (Orissa). Int. J. Pharmocol. 32: 274-283.
- [28] Guyton AC 1991. In: Textbook of Medicinal Physiology, 8th ed. Saunders An imprint of Elsevier. The Curtis Centre Independence Square West, Philadelphia. 390.
- [29] Hong Nie, Lan-zhenMeng, Zhang Hui, Zhang Jian-yu, Zhen Yin and Huang Xue-Song 2008. Analysis of anti-platelet aggregation components of *Rhizomazingiberis* using chicken thrombocyte extract and high performance liquid chromatography. Chin. Med. J. 121(13):1226-1229.
- [30] IizukaT, Moriyama H and Nagai M (2006). Vasorelaxant effects of methyl brevifolin carboxylate from the leaves of *Phyllanthusniruri*. Biol. Pharm. Bull. 29(1): 177-179.
- [31] Jackson SP, Nesbitt WS and Kulkarni S 2003. Signaling events underlying thrombus formation. J. Thromb. Haemost. 1:1602–1612.
- [32] JinY R, Han XH, Zhang YH, Lee JJ, Lim Y, Chung JH and Yun YP 2007. Antiplatelet activity of hesperetin, a bioflavonoid, is mainly mediated by inhibition of PLC-γ2 phosphorylation and cyclooxygenase-1 activity. Athero. 194: 144-152.
- [33] Lee JJ, Jin YR, Lim Y, Hong JT, Kim TJ, Chung JH and Yun Y P. 2006. Antiplatelet activity of carnosol is mediated by the inhibition of TXA2 receptor and cytosolic calcium mobilization. Vasc. Pharmacol. 45: 148–153.
- [34] Lin TJ, Su CC, Lan CK, Jiang DD, Tsai JL and Tsai MS (2003). Acute poisonings with Breyniaofficinalis-an outbreak of hepatotoxicity. J. Toxicol. Clin. Toxicol. 41: 591-594.

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