

# A Review on Ayurvedic and Pharmacological Properties of Patalgarudi (Cocculus hirsutus (L.) W.Theob.)

Shr<mark>eya</mark>sh S<mark>hind</mark>e <sup>1</sup>

Satish Pakanikar<sup>2</sup>

1 Assistant Professor

2Associate Professor and HOD

Department of Dravyaguna Vigyan, Sai Ayurved College-Hospital and Research Centre Sasure - Vairag - Solapur

**Abstract: Background:** Patalgarudi (Cocculus hirsutus (L.) W. Theob.) (Menispermaceae) is an Ayurvedic medicinal plant which is not mentioned in Ayurvedic classical books but mentioned in latest Nighantus (Plant Encyclopedia ) like Bhavprakash, Rajnighantus etc. According to Ayurveda this plant is having Guna- Sheet Ras-Katu, Veerya-Ushna, Vipaka-Katu, Vaatahar and Kaphahar. Many pharmacological studies have been conducted to investigate the properties of **Patalgarudi** (Cocculus hirsutus (L.) W.Theob.) in an attempt to authenticate its use as a multi-purpose medicinal agent. The main aim of this article is to collect and analyze the scientific information related to traditional uses, bioactive chemical constituents and pharmacological activities. Methods: Scientific information on Patalgarudi C. hirsutus was retrieved from the online bibliographic databases (e.g. MEDLINE/PubMed, SciFinder, Web of Science, Google Scholar and Scopus) and books from central library as well as library of Dravyaguna department of Sai Ayurved College, Hospital and Research Centre Sasure-Vairag-Solapur. Results: According to Ayurveda Patalgarudi it is effective against visha (poison), Rakta-shuddhikar( blood purifier), it is spermatogenic taken with sugar and black piper regularly. Different plant parts of *Patalgarudi C. hirsutus* were reported to be used for the treatment of fever, skin diseases, stomach disorders and urinary diseases. Alkaloids such as jasminitine, hirsutine, cohirsitine and their derivatives along with a few flavonoids, triterpene derivatives and volatile compounds were reported from whole plant or different plant parts. Extracts were evaluated for their antimicrobial, antidiabetic, immunomodulatory and hepatoprotective activities among others. Conclusion: The mechanisms of action for these properties are not fully understood. Preliminary studies have found various constituents of Patalgarudi (Cocculus hirsutus (L.) W.Theob.) exhibiting a variety of therapeutic effects. These results are very encouraging and indicate this herb should be studied more extensively to confirm these results and reveal other potential theraSpeutic effects.

Keywords: Patalgarudi Cocculus hirsutus; Menispermaceae;; Ayurvedic uses; alkaloids; pharmacological activity

**1INTRODUCTION**: *Patalgarudi* (*Cocculus hirsutus* (*L.*) *W.Theob.*) is commonly known as Vasan vel in Marathi, Jal-jamani in Hindi and Broom-Creeper in English .It is slender climber with hairy leaves. This plant can be found in dry areas during and after the monsoon. This plant is belongs to Menispermaceae family. The Menispermaceae family consists of about 70 genera and 500 species .¹ Amongthem, the genus Cocculus comprises about 10 species distributed in Asia, Africa, Australia and North America. ¹ Cocculus hirsutus (*L.*) W.Theob (syn. Cebatha hirsuta (*L.*) Kuntze, Cebatha villosa C.Chr., Cocculus aristolochiae DC., Cocculus hastatus DC., Cocculus hirsutus (*L.*) Diels, Cocculus holopeira-torrida Broun & R.L.Massey, Cocculus linnaeanus Kurz, Cocculus sepium Colebr., Cocculus villosus DC., Menispermum hirsutum *L.*)² is a perennial climber distributed mostly in tropical and subtropical areas .³ In Asia, it is reported from India, Myanmar, Nepal and Pakistan and southern China <sup>4-6</sup>. This plant is used from time immemorial for the treatment of various diseases across India ,Africa and China. In various part of India , tribal and rural population still use this plant for the treatment of gynecological problems, weakness and bleeding disorders .

## **2 HISTORICAL REVIEW**

According to Ayurveda its Rasapanchak of Patalgarudi is

Ras(taste) -Tikt(bitter),

Gun(qualities) -Laghu(light to digest), Picchil (Sticky)

Vipak(metabolism) -Katu (undergoes pungent taste after digestion)

Veerya (potency) -Sheet (cold)
Karm -Vaat-Kaphaghna

Patalgarudi is indicated for raktshuddhi (blood purification) ,spermatogenesis, Dhahaghna (for coldness of the skin), Vishaghna (anti poison)

Varius uses of Patalgarudi is mentioned in Raaj-Nighantu and Bhavprakaash -Nighantu

#### 3 BOTANICAL DESCRIPTION

Broom-creeper is a climbing undershrub, often densely velvety. Leaves are 4-8 cm long, 2.5-6 cm broad or ovate-oblong, sometimes 3-5 lobed, base heart shaped, wedge-shaped or flat, tip blunt or with a small point. Leaves are densely velvety when young, later nearly hairless. Basal nerves are 3-5. Leaf stalk is 0.5-2.5 cm long. Male flowers have sepals hairy, the outer 3, oblong-lanceshaped, 1.5-2 mm long.0.5-0.8 broad, the inner 3 broadly ovate, 1.5-2.5 mm long, 1.7-2 mm broad. Petals are ovate-oblong, 0.5-1.5 mm long, 0.3-6 mm broad. Stamens are 0.7 – 1 mm long. Female flowers 1-3, on axillary stalks, rarely racemed. Perennial climber 2-3.Leaves 3-5 veined from the base, variable in shape, older leaves often distinctly 3-5 lobed, younger leaves oblong- ovate to somewhat obovate, covered in yellowish velvety hairs, apex with a small with a sharp mucro. Flowers in axillary clusters, unisexual, sepals densely hairy. Fruit somewhat ellipsoid, 4 mm in diameter, freshy, purple-bluewhen ripe. Fruit is a dark purple berry, 4-8 mm long, 4-5 mm broad, endocarp annular or ribbed with a prominent dorsal crest, performed. The juice of the ripe fruityields a permanent bluish-purple ink and the roots as well as the leaves are used in native medicine. Flowering-December- March <sup>7</sup>

## 4 BOTANICAL CLASSIFICATION 8

• Kingdom: *Plantae* 

Subkingdom: *Tracheobionata* Division: *Magnoliophyta* Subdivision: *Spermatophyta* Class: *Magnoliopsida*

Subclass: *Magnolidae* Order: *Ranunculales* Family: *Menispermaceae* 

• Genus: Cocculus

• Species: Cocculus hirsutus

#### 5 VERNACULAR NAME9

Sanskrit-Patalgarudi, Dirghavalli, Vastadani Hindi-Jal-jamani, Jamti ki bel Marathi-Vaasanvel Telagu-Dusara teega Kannada-Soggadivalli Gujarati-Vevati Tamil-Kattukkodi

#### 6 CHEMICAL CONSTITUENTS

The plant of *C.hirsutus* has been reported to contain essential oil,  $\beta$ - sitosterol, ginnol, glycosides, sterols and alkaloids<sup>10-11</sup>. Preliminary phytochemical analysis of the leaves showed presence of alkaloids, phenolic compounds, flavonoids, glycosides, and carbohydrates. The phytochemical studies show the presence of bis-benzyl isoquinoline alkaloids; viz. shaheenine<sup>12</sup>, cohirsinine<sup>13</sup>, hirsutine<sup>14</sup>, jamtinine<sup>15</sup>, jamitine-N-oxide<sup>16</sup>, cohirsine <sup>17</sup>, Cohirsitine <sup>19</sup> and haiderine<sup>18</sup> which are isolated from stem and roots. The alkaloids present in the leaves of *C.hirsutus* are Dtrilobine and DL-coclaurine, isotrilobine, (+)syringaresinol and protoquericitol<sup>20</sup>. Roots are reported for the presence of D-trilobine and coclaurine, sterols and resins<sup>21</sup>.

#### **7AYURVEDIC USES:**

According to Ayurveda Root of Patalgarudi is Ushna, Swedjanan, Saumya, Balvardhak, Mutrajanan, Grahi, Jwarahar, Vaathar. Extract made by Root of Patalgarudi when given with Pipper, Ginger is useful in Joint pain, swellings as well as in Rheumatoid arthritis. It is useful in Syphilis. Poltis of leaves is useful in swellings, wounds when applied externally.<sup>22</sup>

#### **8 ETHNOBOTANY**

In Konkan, the roots, rubbed with Bonduc nut, are administered as a cure for belly-ache in Children. The root is generally used as a gentle laxative. It has been extensively used as a alternative in rheumatic and venereal diseases. In Sind, the root and leaves are used in headache and neuralgic pain. The juice of leaves, mixed with water, has the property of coagulating into green jelly like substance, which is taken internally, sweetened with sugar, as cure for gonorrhea. In Baluchisthan the mucilage is used to cure spermatorrhoea, taken in milk; it is used to for cough and to put on to sore eyelid and to soften breasts. 7

## 9 CHEMICAL CONSTITUENTS

Although widely used in traditional medicines and studied well for its pharmacological activities, the chemical constituents of C. hirsutus are not well explored. Earlier studies in 1960s and 1970s have reported the presence of alkaloids through preliminary phytochemical screenings and isolation and identification of a few alkaloids such as trilobine, isotrilobine, coclaurine and magnoflorine <sup>23-25</sup> and other compounds i.e., \_-sitosterol, ginnol and monomethyl ether of inositol. <sup>26</sup> Few studies performed during or after 1980s, have reported several

alkaloids from various plant parts. From whole plant and ethanol extract Jamtinine, <sup>27,28</sup> Haiderine, <sup>28</sup> Hirsutine, <sup>28,29</sup> Cohirsitine, <sup>28</sup> Cohirsitine, <sup>28,30</sup> Cohirsine, <sup>28,31</sup> Cocsuline-*N*-2-oxide t, <sup>32</sup> Cohirsinine, <sup>28,33</sup> are reported. From Stems and roots/ethanol extract Corsutine, <sup>34</sup> Jamtine *N*-oxide, <sup>28,35</sup> Coclaurine, <sup>28,24,25</sup> Shaheenine, <sup>28,29</sup> Magnoflorine s, <sup>28,24</sup> Trilobine, <sup>28,24,25</sup> Isotrilobine s, <sup>28,24</sup> Three flavonoids rutin, liquiritin and quercetin were also reported from the leaves .<sup>35</sup> A triterpene derivative, hirsudiol is also reported from the ethanol extract of whole plant. <sup>36</sup> Similarly, beta sitosterol and 28-acetyl botulin were isolated from the aqueous extract of aerial parts .<sup>37</sup> Many studies have reported the preliminary phytochemical screening of the extracts and presence of carbohydrates, steroids, alkaloids, glycosides, flavonoids, tannins and saponins.<sup>38</sup>

#### 10 PHARMACOLICAL ACTIVITIY

The medicinal traits and pharmacological activities endorsed to various parts of *Coculus hirsutus* are detailed as follows:

a)Antidiabetic: Anti-diabetic effect was observed with *C.hirsutus* when given as an aerial part extract in normal as well as diabetic rats. The effect, however, was more pronounced in diabetic animals in which administration for 15 days after streptozotocin-induced diabetes, significantly reduced blood glucose levels. After streptozotocin induced diabetes, it was observed that both standard drug (glibenclamide) and methanolic extract of *C. hirsutus* were significantly superior to control in reducing blood sugar on long treatment (15 days). *C. hirsutus* could be of benefit in diabetes mellitus in controlling blood sugar<sup>40</sup>. The aqueous extract of leaves of *C.hirsutus* decreased the serum glucose level and improved glucose tolerance. Total alkaloids reduced the blood sugar level of diabetic rats significantly. Hence, the alkaloids in the roots of *C.hirsutus* have been reported to be responsible for the antihyperglycemic activity. The aqueous extract of leaves of *C.hirsutus* has antihyperglycemic activity as it lowers serum glucose level in diabetic mice and significantly increases glucose tolerance. The extract also prevents loss of body weight in diabetic mice.<sup>41</sup> Total alkaloid fraction prepared from methanol extract of roots of *C. hirsutus* showed considerable hypoglycemic activity on alloxan-induced diabetic rats. The thin layer chromatography profile of total alkaloid fraction showed the presence of four alkaloids, whereas butanol fraction showed the presence of steroids and/or triterpenoids.<sup>42</sup>

# b) Diructic and Nephroprotective Activity

Ganapaty et al. studied the diuretic activity of the aqueous extract of the aerial parts of C. hirsutus in normap mice and the extract at a dose of 100 and 200 mg/kg, p.o. showed significant increase in the urinary concentrations of Na+ and K+ suggesting potent diuretic activity. AB adole et al. carried out the acute and chronic diuretic activity of the ethanolic extract of leaves of C. hirsutus in normal rats and the extract significantly increased the urinary concentrations of Na+ and K+44. Gadapuram et al. reported the potent nephroprotective activity of the ethanolic extract of the leaves of C. hirsutus in 5/6 nephrectomized rat model.

# c)Anti-Oxidant Activity

The aqueous extract of the leaves of C. hirsutus using 1,1-diphenyl-2-picrylhydrazyl (DPPH) free radical and reducing power assay, and the extract showed potent DPPH free radical scavenging assay with IC50 values of 2.75 ± 0.3 µg gallic acid equivalents (GAE)/ml and reducing power activity with the value of 65.17± \_ 4.8 U/mg GAE. The extract also showed the total phenolic content of 31.83 ± \_ 3.1 mg GAE/g. Rakkimuthu et al. studied the anti-oxidant activity of C. hirsutus. The results showed potent DPPH free radical scavenging activity, ABTS free radical scavenging activity, nitric oxide scavenging activity, reducing power, inhibition of lipid peroxidation and metal chelating activity assay as ascorbic acid .<sup>47</sup>

# d)Spermatogenic

Testosterone levels in the testes were significantly higher in methanolic extract (both 400 and 800 mg/kg) of *C. hirsutus* treated rats after 15th days of treatment compared to the control group. The chronic treatment of the extract for 15 days has increased in the weight of testis, its diameter and seminiferous tubules. There is also a progress in spermatogenesis and increase in *cauda epididymal* sperm count. The significant increase in the weight of reproductive organs is also indirectly supports the increase availability of androgens. Increased weight and high protein concentration of the testis indicates the enhancement of testicular growth as FSH is essential for protein synthesis in gonads<sup>48</sup>.

## e) Immunomodulatory Activity

The immunomodulatory activity of the combination (1:1, 2:1 and 1:2 ration) of leaves of C. hirsutus and flowers of Sesbania grandiflora (L.) Pers. (Fabaceae) in mice. The 1:1 combination mixture showed potent immunostimulatory activity. Rastogi et al. evaluated the immunostimulatory activity of aqueous and ethanolic extract of aerial parts of C. hirsutus in normal aswell as cyclophosphamide induced immunosuppressed rats. The extracts showed the dose dependent increase in the carbon clearance, humoral antibody (HA) titre, delayed type hypersensitivity (DTH) and white blood cell (WBC) count in a dose dependent manner and authors concluded that the extract was effective to stimulate the immune system and also to protect from the immunosuppressant.

**f)Acute toxicity:** The aqueous extract of *C.hirsutus* aerial parts orally evaluated for the acute toxicity in mice. The lethal dose 50 (LD50) was determined. The acute toxicity was found to be higher than 3000 mg/kg.<sup>51</sup>

# 12) CONCLUSION

*C.hirsutus* is having less reference as a medicine in Ayurvedic literature but having lot of references as a traditional medicine C.hirsutus is rich of chemical constituent, which have therapeutic and medicinal value like alkaloids, phenolic compounds, flavonoids, glycosides, and carbohydrates. C.hirsutus produces anti-inflammatory, antispermatogenic, antidiabetic, antitumour, antimicrobial, diuretic and laxative activity. C.hirsutus has great potential as anti-inflammatory drug and it can play a important role in developing new formulation for treating inflammation, diabetes and enhancing immunity. Still a lot of work to be done for exploring the evidences for use of this plant.

#### 13 REFERENCES

- 1. DeWet, H.; Struwig, M.; VanWyk, B.E. Taxonomic notes on the genus Cocculus (Menispermaceae) in southern Africa. S. Afr. J. Bot. **2015**, 96, 99–104.
- 2. World Flora Online (WFO). Cocculus hirsutus (L.) W.Theob; Published on the Internet. Available online: http://www.worldfloraonline.org/taxon/wfo-0000613546 (accessed on 3 November 2020).

Medicines **2020**, 7, 0069 8 of 10

- 3. Panda, B.R.; Mohanta, S.R.; Mishra, U.S.; Kar, S.; Panda, B.K.; Chakraborty, P. Antibacterial activity of the leaves of Cocculus hirsutus. Indian Drugs 2007, 44, 108–116.
- 4. Shrestha, K.K.; Bhattarai, S.; Bhandari, P. Gymnosperms and Angiosperms: Cycadaceae—Betulaceae. In Handbook of Flowering Plants of Nepal; Scientific Publishers: Jodhpur, India, 2018; Volume 1.
- 5. Ahmad, V.U.; Iqbal, S. Jamtinine, an alkaloid from Cocculus hirsutus. Phytochemistry 1993, 33, 735–736.
- 6. Fahmy, A.G.; El-Bakry, A.A. Phytogeographical significance of Wadi Wateer (Sinai), Egypt, with special reference to Cocculus hirsutus (L.)W.Theob. Plant Syst. Evol. **2011**, 297, 299–303.
- 7 K.R.Kirtikar, B.D.Basu Indian Medicinal Plants-International Book Distributers 2nd Edition 1935 volume 1,86-89
- 8. Chatterjee Tk, "Herbal Options", 1996,1st edition, published by M/s Eastern Traders, Calcutta:157-178
- 9 Nigantu Aadarsha Vol.2 –Bapalal Vaidya 1st edition published by Chaukhambha Bharati Academy Varanasi: 42-43

- 11. Das PK, Nath V, Gode KD, Sanyal AK, Preliminary phytochemical and pharmacological studies of *Cocculus hirsutus* Linn, *Ind. J Med Res*, 1964; 52: 300-307.
- 12. Rasheed T, Khan MN, Zhadi SS, Shaheenine. A new alkaloid from Cocculus hirsutus, Fitoterapia, 1991; 62: 157-158.
- 13. Viquaruddin A, Tahir R, Shaista I, Cohirsinine, an alkaloid from *Cocculus hirsutus*, *Phytochemistry*, 1991,30, 1350-1351.
- 14. Rasheed T, Khan MN, Zhadi SS, Hirsutine, A new alkaloid from cocculus hirsutus. Pak J Nat Prod, 1991; 54:582-584.
- 15. Vigaruddin A, Iqbal S, Jamtinine, An alkaloid from *Cocculus hirsutus*. *Phytochemistry*, 1993(a); 33:735-736.
- 16. Viqaruddin A, Rahman AU, Tahir R, Jamtine- N oxide, A new isoquinoline alkaloid from *Cocculus hirsutus*. *Heterocycles*, 1987(a); 26: 1251-55.
- 17. Viqaruddin A, Rahman AU, Rasheed T, Cohirs<mark>ine:</mark> A new isoquinoline alkaloid from *Cocculus hirsutus*. *Tetrahedron*, 1987b; 43: 5865-5872.
- 18. Viquaruddin A, Iqbal S. Cohirsitine, A new isoquinoline alkaloid from *Cocculus hirsutus*. *Fitoterapia*, 1992; 63:308-310.
- 19. Viqaruddin A, Iqbal S, Haiderine, A new isoquinoline alkaloid from *Cocculus hirsutus Nat Prod Lett*, 1993; 2: 105-109.
- 20. Jagannadha Rao KV, Ramachandra RL, Chemical examination of Cocculus hirsutus (Linn) Diels. J Sci Ind Res, 1961; 20(B): 125-126.
- 21. Vigaruddin A, Tahir RJ, Studies on the chemical constituents of Cocculus hirsutus. Chem Soc Pak, 1986; 8:537-540.
- 22 Bhavprakash Nighantu Commentary by Dr.K.C. Chunekar Chaukhambha Bharati Academy Varanasi 449-450
- 23.. Tripathi, V.J.; Ray, A.B.; Dasgupta, B. Alkaloids of Cocculus hirsutus DC. Indian J. Chem. Sect. B Org. Chem. Incl. Med. Chem. 1976, 14, 62–63.
- 24. Jagannadha Rao, K.V.; Row, L.R.M. Chemical examination of Cocculus hirsutus DC. J. Sci. Ind. Res. 1961, 20b, 125–126.
- 25. Naik, R.M.; Merchant, J.R. Chemical investigation of Cocculus hirsutus. Curr. Sci. 1956, 25, 324–325.
- 26. Merchant, J.R.; Naik, R.M.; Hirwe, S.N. Chemical investigation of Cocculus hirsutus. J. Indian Chem. Soc. 1962, 39, 411–416.
- 27. Ahmad, V.U.; Iqbal, S. Jamtinine, an alkaloid from Cocculus hirsutus. Phytochemistry 1993, 33, 735–736.
- 28. Ahmad, V.U.; Iqbal, S. Haiderine, a new isoquinoline alkaloid from Cocculus hirsutus. Nat. Prod. Lett. 1993, 2, 105–109.
- 29. Rasheed, T.; Khan, M.N.I.; Zhadi, S.S.A.; Durrani, S. Hirsutine: A new alkaloid from Cocculus hirsutus. J. Nat. Prod. 1991, 54, 582–585.
- 30 Ahmad, V.U.; Iqbal, S. Cohirsitinine, a new isoquinoline alkaloid from Cocculus hirsutus. J. Nat. Prod. 1992, 55, 237–240.
- 31Ahmad, V.U.; Atta-ur-Rahman; Rasheed, T.; Habib-ur-Rehman; Khan, A.Q. Cohirsine—A novel isoquinolone alkaloid from Cocculus hirsutus. Tetrahedron **1987**, 43, 5865–5872.
- 32 El-Shabrawy, A.O.; Schi\_, P.L., Jr.; Slatkin, D.J.; Das Gupta, B.; Ray, A.B.; Tripathi, V.J. Cocsuline-N-2-Oxide,
- a New Alkaloid from Cocculus hirsutus DC. Heterocycles 1984, 22, 993.
- 33Ahmad, V.U.; Rasheed, T.; Iqbal, S. Cohirsinine, an alkaloid from Cocculus hirsutus. Phytochemistry 1991, 30, 1350–1351.
- 34. Yadav, S.B.; Tripathi, V. A minor phenolic alkaloid from Cocculus hirsutus Diels. Indian J. Chem.-Sect. B Org.
- Med. Chem. **2005**, 44, 212–214. **35**Ahmad, V.U.; Atta-ur-Rahman; Rasheed, T.; Habib-ur-Rehman. Jamtine-N-oxide—A new isoquinoline alkaloid from Cocculus hirsutus. Heterocycles **1987**, 26, 1251–1255.
- 36. Patil, V.; Angadi, S.; Devdhe, S.; Wakte, P. Recent Progress in Simultaneous Estimation of Rutin, Quercetin and Liquiritin in Cocculus Hirsutus by HPTLC. Res. J. Pharmacogn. **2015**, 2, 49–55.
- 37. Ahmad, V.U.; Mohammad, F.V.; Rasheed, T. Hirsudiol a triterpenoid from Cocculus hirsutus. Phytochemistry 1987, 26, 793–794.
- 38. Iyer, S.V.; Shankul, K.; Parikh, P.M. Isolation of phytoconstituents from the aerial parts of Cocculus hirsutus Linn. J.Pharm.Res. **2011**, 4, 1946–1947.
- 39. Meena, M.K.; Singh, N.; Patni, V. Determination of bioactive components of the leaves of Cocculus hirsutus (L.) Diels using GC-MS analysis. Int. J. Pharm. Pharm. Sci. **2014**, 6, 327
- 40. Sangameswaran, B, Jayakar, B, Antidiabetic and spermatogenic activity of Cocculus hirsutus, Afri. J. Biotech., 2007; 6(10):1212-1216.

- 41. Badole S, Patel N, Bodhankar S, Jain B, et al. antihyperglycemic activity of aqueous extract of leaves of *Cocculus, hirsutus (L.) Ind. J Pharmacol*, 2006; 38(1):49-53.
- 42. Satyanarayana K, Mangathayaru V, et al. Studies on hypoglycaemic and cardiotonic effects of roots of *Cocculus hirsutus*. *J Pharmaceutical Sci*, 1994; 3: 30-35.
- 43. Ganapaty, S.; Dash, G.K.; Subburaju, T.; Suresh, P. Diuretic, laxative and toxicity studies of Cocculus hirsutus aerial parts. Fitoterapia 2002, 73, 28–31. 44. Badole, S.L.; Bodhankar, S.L.; Patel, N.M.; Bhardwaj, S. Acute and chronic diuretic e\_ect of ethanolic extract of leaves of Cocculus hirsutus (L.) Diles in normal rats. J. Pharm. Pharmacol. 2009, 61, 387–393.
- 45. Gadapuram, T.K.; Murthy, J.S.N.; Rajannagari, R.R.; Kandati, V.; Choda, P.K.; Shukla, R. Nephroprotective activity of cocculus hirsutus leaf extract in 5/6 nephrectomized rat model. J. Basic Clin. Physiol. Pharmacol. 2013, 24, 299–306.
- 46. Srikanta, B.M.; Dharmesh, S.M. Anti-Helicobacter pylori, proton pump inhibitory and antioxidant properties of selected dietary/medicinal plants. Int. J. Phytomed. 2012, 4, 573–581.
- 47. Rakkimuthu, R.; Kavithakrishna, R.; Suganyadevi, P.; Aravinthan, K.M. Quantitative phytochemical analysis and their antioxidant activity of Cocculus hirsutus (1.) Diels fruit. Int. J. Phytomedicine 2012, 4, 447–455.
- 48. Sangameswaran, B, Jayakar, B, et al. Antidiabetic and spermatogenic activity of *Cocculus hirsutus*, *Afri. J. Biotech.*, 2007; 6(10):1212-1216.
- 49. Mallik, A.; Nayak, S. Study the Immunomodulatory Effects of Combined Extracts of Sesbania grandiflora Flowers and Cocculus hirsutus Leaves on the Circulating Antibody Response. Am. J. Phytomed. Clin. Ther. 2015, 3, 199–208.
- 50. Rastogi, B.; Tiwari, U.; Dubey, A.; Bawara, B.; Chauhan, N.S.; Saraf, D.K. Immunostimulant activity of Cocculus hirsutus on immunosuppressed rat. Pharmacologyonline 2008, 3, 38–57.
- 51. Ganapaty S, Dash GK, Diuretic, laxative, toxicity studies of *Cocculus hirsutus*, *Fitoterapia*, 2002;73 (1):28-31.

