International Journal of Pharmacy and Medicine Sciences
Vol. 2, Issue 3, March 2026
ISSN: 3108-009X

Open Access REVIEW

The Dual Face of *Aristolochia indica*: Anti-Inflammatory Promise and Toxicological Challenges -A Review

[1]*Syamjith P., [2]Muhammed Shakeeb, [3]Ms. Nandana T, [4]Navya M, [5]Nandana A, [6]Anson S. Maroky, [7]Muhammed Mansoor, [8]G. Babu

[1*]Associate Professor, Department of Pharmacology, Devaki Amma Memorial College of Pharmacy, Kerala
[2,3,4,5]Students. Devaki Amma Memorial College of Pharmacy, Kerala
[6]Professor and Head, Department of Pharmacology, Department of Pharmacology, Devaki Amma Memorial College of Pharmacy, Kerala
[7,8]Principal, Pharmacology, Devaki Amma Memorial College of Pharmacy, Kerala

***Submission**: Feb. 19, 2026; **Revised: March** 23, 2026; **Published**: March 31, 2026*

Corresponding author:
Syamjith P.
Associate Professor, Department of Pharmacology, Devaki Amma Memorial College of Pharmacy, Kerala
Email id: syamvzr@gmail.com@gmail.com

A B S T R A C T

Aristolochia indica, a perennial medicinal shrub belonging to the *Aristolochiaceae* family, is widely distributed across the tropical and subtropical regions of the Indian subcontinent. Historically utilized since the Graeco-Roman era, this endangered plant is valued in traditional medicine for treating cholera, inflammation, and snake bites. Modern pharmacological evaluations have confirmed its significant antioxidant and anti-diabetic potential, primarily attributed to bioactive constituents like flavonoids, and terpenoids. Specifically, various extracts demonstrate dose-dependent ROS-scavenging activity and effective blood glucose reduction in diabetic models. However, the therapeutic utility of *Aristolochia indica* is severely constrained by the presence of aristolochic acids (AAs), which are potent nephrotoxins and carcinogens. Clinical evidence links AA exposure to aristolochic acid nephropathy (AAN), upper tract urothelial carcinoma (UTUC), and increased risks of hepatocellular carcinoma. Given these toxicological risks, future research must prioritize the development of AA-free antioxidant fractions. Comprehensive pharmacokinetic profiling and mechanistic studies on its neuroprotective and anti-inflammatory pathways are essential to safely bridge traditional knowledge with evidence-based modern pharmacotherapy.

Keywords: *Aristolochia indica*, Aristolochic acid, Antioxidant activity, Nephrotoxicity, Anti-diabetic.

INTRODUCTION

Aristolochia indica, one of the 500 species of the family *Aristolochiaceae* is distributed throughout the tropical, subtropical and Mediterranean regions. In Indian subcontinent, the plant is found in low hills and plains of India from Nepal and lower Bengal to Chittagong in Bangladesh and Coromondal Coast [1][2]. *A. indica L.*, a member of the *Aristolochiaceae* family, is referred to as Ishwar balli in Kannada, Indian Birthwort in English, Isharmul in Hindi, and Ishwari in Sanskrit. Locally called Isharmul (Bengali and Hindi), this shrub has a lengthy twinning stem and is an endangered medicinal plant. Aristolochic acid, a component of *Aristolochia* species, has been utilized medicinally since the Graeco-Roman era. The plant is used to treat cholera, fever, intestinal difficulties, ulcers, dangerous bites [3]. It is also utilized as emmenagogue, abortifacient, antineoplastic, antiseptic, anti-inflammatory, antibacterial and phospholipase A2 inhibitor [4][5].

Botanical and Taxonomical Description of *Aristolochia indica*

Taxonomical Classification

Table No.1. Taxonomical classification *A. indica* [6]

Kingdom	**Plantae**
Phylum	Tracheophyta
Class	Magnoliopsida
Order	Piperales
Family	*Aristolochiaceae*
Genus	*Aristolochia L.*
Species	*Aristolochia indica*

Common Name

Table No. 2. Common names in different colloquial term for *A. indica* [6]

Karalakam	Malyalam
Aadagam, Arkmula	Gujarati
Eshwawara mooli, Esvaraveru	Telegu
Isvaramul	Tamil
Arka mula	Assam
Isharamool	Nepali
Isaraberu	Tulu
Hooka-bel	Hindi

Habitat and Distribution

Southern India, Nepal, Sri Lanka, and Bangladesh are home to the creeper plant *A. indica* [7]. The plant is found in Bengal, Assam, and the lower hills and plains of India.

Botanical Description

The genus *Aristolochia (Aristolochiaceae)* contains more than 500 species, the majority of which are found in tropical and subtropical climates in the Mediterranean region of the world. The perennial creeper *A. indica* has a woody rootstock.

Root: Tap root, long, cylindrical, branched, unevenly bent, 3 to 10 mm in diameter; smooth, coarsely wrinkled, grayish-brownish exterior; white interior; short, splintery fractures; unique flavor and odor. Stem: Twining, thin, woody at base, grooved, glabrous, brownish on the exterior, smooth, finely wrinkled, white inside, short, splintery fracture, taste strongly of bitterness, unique odor.

Leaf: Simple, alternating, round, sub-truncate or subcordate, cuneate at the base, 3.5 to 12.5 cm long, 1.5 to 7.5 cm broad, bitter-tasting, with a distinctive smell. Oblong or subpanduri form, obtusely acuminate, whole with moderately undulate margin. Lackluster.

Floral characteristics include a few flowered axillary racemes, small, ovate, acuminate bracts opposite the pedicels, a long, thickened pedicel above, a greenish-white perianth up to 4.5 cm long with a globose inflated base bent at a right angle, and a sudden narrowing into a cylindrical tube with an oblique trumpet-shaped mouth that gradually passed into a long, narrow, linear-oblong, obtuse brownish lip. 6 anthers, 6 lobes in style.

Fruit: A 4 to 5 cm long capsule with an oblong or globose-oblong opening at the top, six valves, and a pedicel that splits into six filaments.

Seed: According to Faisal, Mohammed, et al. (2015), the seed is ovoid, sharp, flat, winged, and deltoid.

Phytochemical Composition of *Aristolochia indica*

Alkaloids, tannins, cardiac glycosides, steroids, flavonoids, and saponins have all been found in the plant according to preliminary phytochemical investigation [8]. The following phytochemical constituents can be found in different parts of *A. indica*.

Aerial part

a) ß-Caryophyllene, α-Humulene, Ishwarone, Caryophyllene oxide I, Ishwarol, Linalool, αTerpinolene, Ishwarane, Aristolochene, Cis-3-Hexenol, Germacrene D, Octen-3-ol, 3- Hexenyl acetate, Camphor, Nonanol, Humulene oxide, Nerolidol, ß-Farnesene, ßBisabolene, Pinocarveol, δ-Cadinol, ß-Elemene, α-Terpineol, ß-Farnesol, Octanol, Caryophyllene oxide II, α-Bisabolol, Germacrene A, Ledol, 2- Octanol, Hexyl acetate, Thymol, Indole, ß-Phellandrene, Tetradecanol, 5ßH,7ß,10α-selina4(14),11-diene, ß-Pinene, Borneol, Terpinene-4-ol, ß-Selinene, Hexanol, (12S)-7, 12- Secoishwaran-12-ol, Camphene, Tricyclene [9].

b) Astragalin, (-) hinokinin, Aristolochic acid I, Aristolactam I, Aristolochic acid II [10].

Root

a) Aristololactam N-ß-D-glucoside, 3ß-hydroxy-stigmast-5-en-7-one, 6ß-hydroxy-stigmast-4- en-3-one.

b) Aristolochic acid I, Aristolochic acid-D, Methyl Aristolochate, Aristolactam-A II, Aristolactam I, Aristolactam, Aristolactam-C N-ß-D Glucoside, Aristolactam ß-D Glucoside [11].

Stem

a) α-pinene, Camphene, ß-pinene, p-cymene, Limonene, trans-pinocarveol, Pinocarvone, Terpinen-4-ol, Myrtenol, Myrtenal, Carvone, α -terpinyl acetate, Aromadendrene, (E)-ßionone, α –cadinol.

Stem and leaf

a) Aristolochic acid I, Aristolochic acid II, Aristolochic acid IV, Aristolochic acid D, Aristolochic acid IIIa, Aristolochic acid Ia, Cepharadione A, Aristolactam I; N-ß-Dglucopyranoside, Aristolactam AII, Aristolactam III, Aristolactam I, AristolactamIVa, Aristolactam AIII, Aristolactam II, Aristolactam II; N-ß-D-glucopyranoside, Aristolactam IIIa; N-ß-D-glucopyranoside, Aristolactam Ia; N-ß-D-glucopyranoside, Aristoloterpenate I, Ariskanin B, 9-Methoxyaristolactam II, Norcepharadione A [12].

Protective Manifestations of *Aristolochia Indica*

Anti-oxidant activity

An *in vitro* study of subramaniyan et al., 2015 give clear evidence on antioxidant property of *A. indica*, In vitro antioxidant property with aqueous and chloroform extracts utilising several free radical models such as hydrogen peroxide (H_2O_2), DPPH radical scavenging and reducing power assay. The chloroform extract of the plant displayed promising antioxidative property and phytochemical screening disclosed the presence of phenol, tannins, saponins, flavonoids and glycosides in chloroform and aqueous extract which might be responsible for their mighty antioxidant activity of *A. indica* [13].

The ethyl alcohol extracts of leaves and flower were used to screen radical scavenging efficacy by DPPH free radical scavenging assay. Leaf extract scavenges DPPH radicals more efficiently as compared to flower extract [14]. Karan et al., 2012 studied in vitro anti-oxidant property of *A. indica* by using DPPH radical and superoxide anion radical scavenging in concentration dependent manner. Curcumin and vitamin C used as standard in superoxide and DPPH assay respectively. Chloroform extract of the aerial part of *A. indica* contain rich source of natural antioxidants [15].

A study of evaluation of antioxidant property of *A. indica* using Phosphomolybdenum method which indicate that methanolic extract of leaves of *A. indica* possess higher total antioxidant capacity (TCA) which is expressed as ascorbic acid equivalent and estimated total phenolic content [16]. Scientists reported

antioxidant property due to presence of vital compound terpenoids in *A. indica* by 2,2-reducing power, DPPH radical scavenging activity, total polyphenol estimation, and ammonium thiocynate assay using various extract of plant like ethyl acetate, petroleum, and chloroform. Another study shows *A. indica* extract with different concentration (100 µg/ml, 200 µg/ml, 300 µg/ml, 400 µg/ml, 500 µg/ml)has a dose dependent antioxidant property evaluated by ferric reducing antioxidant power (FRAP) assay and DPPH assay, Extract shows high level of scavenging Activity at 500 µg/ml with radical scavenging activity of 73.06 %. Similarly, Gouri Rani Baglary et al., 2025 reported *A. indica* has high level phenolic content and possess remarkable Antioxidant activity by using DPPH, FRAP and ABTS method. Report of many research clear that *A. indica* possess antioxidant property [17].

Anti-diabetic activity

The active component Stigmast-5-en-3ß-ol (ß-sitosterol) was isolated from the chloroform extract of *A. indica* show that excellent antihyperglycemic activity as it lowers the serum glucose level in alloxan induced diabetic mice [18]. Goverdhan et al. 2008 indicates the antihyperglycemic effect of methanolic and alcoholic extract of root of *A. indica*. Studied performed in alloxan-induced diabetic mellitus in Sprague Dawley rats. The result was compared with a standard oral hypoglycemic drug glibenclamide, the methanolic extract reduced blood glucose level in normal rat shows antihyperglycemic effect dose dependently and alcoholic extract orally administered in different dose shows reduced blood glucose level in rat as compared to control group [19].

A study of antihyperglycemic activity of ethanolic extract of *A. indica* root in streptozotocin-nicotinamide induced diabetic rats give a clear significant decline in blood glucose level in fasting blood sugar level with different dose and repeated oral administration when compare to standard glibenclamide treated group and control group, Antihyperglycemic effect is dose and duration of administration dependent [20]. *A. indica* rich in phenol, flavonoids [13], terpenoids and particularly ß-sitosterol [18] shows Antioxidant activity. So, antidiabetic activity of *A. indica* by antioxidant property.

Toxicodynamic Impact of *Aristolochia Indica*

Nephrotoxicity

Most of the plants species from Arristolochia genus contain Aristolochic acid (AAs). Aristolchic acids can cause renal failure and mutagenicity. Renal failure along upper tract urothelial carcinoma (UTUC) seen in female patient taking slimming drugs can caused by Aristolichic acid derived adducts of DNA and mutational transformation of A→T characteristically while complete mechanism is not clearly understood [21].

The renal failure was typified by excessive interstitial fibrosis with atrophy, tubule loss, and urothelial hyperplasia, primarily in the superficial cortex. UTUC primerly seen as the urethelial atypia and atypical hyperplasia which then progressed to urotheilal carcinoma on upper tract of urinary tract [22]. After this discovery some scientists said this Aristolchic acid nephropathy (AAN) have some similarity to the Balkan Endemic Nephropathy's clinical and morphological features [23][24].

The use of AA-containing products has lowered the incidence of urothelial carcinoma in individuals with end-stage renal failure. The death rate from these malignancies is significant. The cumulative exposure to AAs is linked to urothelial carcinomas, which are primarily of the synchronous bilateral or metachronous contralateral variety. Furthermore, TP53 mutations and AA-derived DNA adducts are clinically significant to investigate the role of AAs in UTUC [25][26][27].

Hepatotoxicity

Aristolochic acids (AAs) are different nitrophenanthrene carboxylic acids. Other than nephrotoxicity AAs also display other organ cancer like in liver [28]. AA-containing herbs are clinically thought to increase the incidence of hepatocellular cancer in people infected with the hepatitis B virus (HBV) [29]. Analysis of genomic heterogeneity offers compelling proof that AAs may play a role in the onset of liver cancer [30].

Even though a number of distinct processes have been hypothesized, the precise molecular mechanism behind AA-induced hepatotoxicity or liver cancer is still mostly unclear [31] and some of these mechanism are AAI-induced acute HPAs in the canine liver may be regulated via the IL6R/NF-κB and c-Myc/Lin28B/let-7 signaling pathways, since IL6R/NF-κB signaling enhances Lin28B/let-7 alterations in the liver brought on by brief AAI exposure, Ras/Raf signaling pathway and PI3K-AKT signaling pathways [32][33][34].

Future Research Perspectives

To ensure safe therapeutic applications, future research on *A. indica* should focus on extracting and characterizing antioxidant fractions that are devoid of aristolochic acid. More research is needed to identify

the specific antioxidants and understand how they reduce oxidative stress in neuronal, reproductive, inflammatory, and cancer-related pathways. In vitro and in vivo studies should be conducted to identify how these antioxidants influence ROS-mediated inflammatory signaling, as well as their ROS-scavenging and redox-regulatory impacts on cancer cell proliferation, death, and metastasis.

The potential of these compounds to enhance chemotherapeutic efficacy or mitigate oxidative stress–driven tumor progression should also be evaluated using appropriate cellular and animal models. Mechanistic studies should investigate neuroprotective effects, including cholinergic regulation, mitochondrial preservation, and synaptic integrity, employing both neuronal cell culture systems and in vivo neurobehavioral models. Complementary in vivo studies assessing learning, memory, and neurotransmitter modulation can further validate their cognitive-enhancing potential. Pharmacokinetic evaluations, including ADME profiling and determination of biological half-life, are essential to understand the systemic behavior and bioavailability of antioxidant constituents. Furthermore, research on herb-drug interactions and safe dose ranges, undertaken using both in vitro enzyme assays and in vivo animal models, will aid in the creation of safe and effective antioxidant-based formulations of *A. indica* for future clinical use. Similarly, a gap for deep evaluation of nootropic and neuroprotective activity of *A. indica* in both in-vitro and in-vivo.

CONCLUSION

Aristolochia indica, a perennial medicinal shrub, is found throughout India's tropical and subtropical areas. It includes several bioactive chemicals, such as aristolochic acids, flavonoids, tannins, saponins, terpenoids, and ß-sitosterol. These phytochemicals contribute to a variety of pharmacological actions, including antioxidant, anti-diabetic, anti-inflammatory, antibacterial, and anticancer properties. In vitro investigations utilizing different extracts revealed significant ROS-scavenging and free radical neutralizing properties. Terpenoids, phenolics, and flavonoids are most likely responsible for the antioxidative benefits. ß-sitosterol and related substances exhibit significant antihyperglycemic and antioxidant properties. Future research should focus on extracting aristolochic acid-free fractions to assure safe medicinal uses. To understand the mechanisms underpinning ROS-mediated signaling modulation, both in vitro and in vivo experiments are required. Neurobehavioral, neuroprotective, and neurotransmitter research can support its cognitive-enhancing potential. Pharmacokinetic assessments, such as ADME profiling and half-life determination, are critical for understanding systemic behavior. Herb-drug interaction research and safe dosage assessments will aid clinical translation. Comprehensive mechanistic investigation will reveal its involvement in apoptosis, proliferation, and metastasis regulation. Overall, *A. indica* shows promise as a source of safe antioxidant-based therapeutics. Its use into modern medicine necessitates comprehensive scientific confirmation to connect traditional wisdom with evidence-based pharmacotherapy. Investigate, the potential of *A. indica*'s antioxidant fractions in mediating neuroprotective and nootropic effects, their role in modulating oxidative stress-driven inflammatory and anticancer pathways.

ABBREVIATIONS

- *A. indica* – *Aristolochia indica*
- mm – millimetre
- cm – centimetre
- N-ß-D- – nitrogen-linked ß-D-glycoside
- DPPH – 2,2-diphenyl-1-picrylhydrazyl
- FRAP – Ferric Reducing Antioxidant Power
- ABTS – 2,2′-azinobis-(3-ethylbenzothiazoline-6-sulfonic acid)
- TAC – Total Antioxidant Capacity
- H_2O_2 – Hydrogen peroxide
- ROS – Reactive Oxygen Species
- in vitro – Experiments performed outside a living organism
- in vivo – Experiments performed in living organisms
- AAs – Aristolochic acids
- UTUC – Upeer tract urothelial carcinoma
- DNA – Deoxyribonucleic Acid
- A→T – Adenine to Thymine transversion mutation
- AAN – Aristolochic Acid Nephropathy
- BEN – Balkan Endemic Nephropathy
- AA – Aristolochic Acid

- TP53 – Tumor Protein 53 (tumor suppressor gene)
- HBV – Hepatitis B Virus
- HPAs – Hepatic Preneoplastic Alterations
- IL6R – Interleukin-6 Receptor
- NF-κB – Nuclear Factor kappa B
- c-Myc – Cellular Myc (oncogene)
- Lin28B – Lin-28 Homolog B
- let-7 – Lethal-7 microRNA
- Ras – Rat Sarcoma (proto-oncogene)
- Raf – Rapidly Accelerated Fibrosarcoma (proto-oncogene)
- PI3K – Phosphoinositide 3-Kinase
- AKT – Protein Kinase B

CONFLICT OF INTEREST

Authors declare for none conflict of interest.

REFERENCES

[1]. Murugan, R., K.R. Shivanna and R.R. Rao. Pollination biology of *Aristolochia tagala*, a rare species of medicinal importance. Curr. Sci., 2006; 91: 795-798.

[2]. Kanjilal, P.B., R. Kotoky and M. Couladis. Chemical composition of the stem oil of *Aristolochia indica L*. J. Essential Oil Res., 2009; 21: 1-2.

[3]. Krishnaraju, A.V., T.V.N. Rao, D. Sundararaju, M. Vanisree, H.S. Tsay and G.V. Subbaraju. Assessment of bioactivity of Indian medicinal plants using Brine shrimp (Artemia salina) lethality assay. Int. J. Applied Sci. Eng., 2005; 3: 125-134.

[4]. Achari, B., S. Chakrabarty and S.C. Pakrashi. An N-glycoside and steroids from Aristolochia indica. Phytochemistry, 1981; 20: 1444-1445.

[5]. Das, R., A. Kausik and T.K. Pal. Anti-inflammatory activity study of antidote *Aristolochia indica* to the venom of Heteropneustes fossilis in rats. J. Chem. Pharm. Res., 2010; 2: 554-562.

[6]. Sreelakshmi K. P, Arya. A, Delna. M. S, Megha Balakrishnan. K, Sandra. P. D. A Comprehensive Review on *Aristolochia indica and Boerhavia diffusa*: Ethnomedical uses, Phytochemistry and Pharmacological Effects, 2024; 11(5).

[7]. Ved D K, Suma Tagadur Sureshchandra, Vijay Barve, Vijay Srinivas, Sathya Sangeetha, K. Ravikumar, Kartikeyan R., Vaibhav Kulkarni, Ajith S. Kumar, S.N. Venugopal, B. S. Somashekhar, M.V. Sumanth, Noorunissa Begum, Sugandhi Rani, Surekha K.V., and Nikhil Desale. 2016. FRLHT's ENVIS Centre on Medicinal Plants.

[8]. Vaghasiya, Y. and S.V. Chanda. Screening of methanol and acetone extracts of fourteen Indian medicinal plants for antimicrobial activity. Turk. J. Biol., 2007; 31: 243-248.

[9]. Jirovetz L, Buchbauer G, Puschmann C, Fleischhacker W, Shafi PM, Rosamma MK. Analysis of the essential oil of the aerial parts of the medicinal plant *Aristolochia indica Linn*. (Aristolochiaceae) from South India. Sci Pharm, 2000; 68: 309-316.

[10]. Desai DC, Jacob J, Almeida A, Kshirsagar R, Manju SL. Isolation, structural elucidation and anti-inflammatory activity of astragalin, (-) hinokinin, aristolactam I and aristolochic acids (I & II) from *Aristolochia indica*. Nat Prod Res., 2014; 28(17): 1413-1417.

[11]. Mix DB, Guinaudeau H, Shamma M. The aristolochic acids and aristolactams. J Nat Prod, 1982; 45(6): 657-666.

[12]. Michl J, Jennings HM, Kite GC, Ingrouille MJ, Simmonds MSJ, Heinrich M. Is aristolochic acid nephropathy a widespread problem in developing countries? A case study of *Aristolochia indica L.* in Bangladesh using an ethnobotanical-phytochemical approach. J Ethnopharmacol., 2013; 149(1): 235-244.

[13]. Subramaniyan, V., Saravanan, R., Baskaran, D., & Ramalalingam, S. 2015. In vitro free radical scavenging and anticancer potential of *Aristolochia indica* against MCF-7 cell line. International Journal of Pharmacy and Pharmaceutical Sciences, 2015; 7(6): 392-396.

[14]. S. Naik, A., Siddiqua, S., M.N, S., Kumari L, S., Kekuda T.R, P. and H.L, R. 2015. Antimicrobial and Radical adical Scavenging Efficacy of Leaf and Flower F of Aristolochia indica Linn. Journal of Science, Technology and Arts Research, 2015; 4(1): 103-108.

[15]. Geetha, Sethupandian & Irulandi, Kokkaiah & Palanichamy, P. Mehalingam. Assessment of the Radical Scavenging Activity and Total phenolic content of Crude Methanolic leaves Extract of Aristolochia indica L.- Aristolochiaceae. Journal of advanced applied scientific research, 2021; 1: 59-66.

[16]. Bhadra, Aratrika & Bt, Manjunath. In-vitro antioxidant analysis of Aristolochia indica, Ipomoea obscura, Tylophora indica, Glinus oppositifolius and Abroma augustum from Bankura district, West Bengal. Journal of Integrated Science and Technology, 2025; 13: 1-8.

[17]. Gouri Rani Baglary, Rangina Brahma, Manisha Hazarika, Anuck Islary, Santosh Kumar. Exploring the phytochemical composition, nutritional profile, and functional properties of different parts of Aristolochia indica and Clerodendrum chinense, Food and Humanity, 2025; 5: 100655.

[18]. Karan, Sanjay & Mishra, Sagar & Pal, Dilipkumar & Mondal, Arijit. Isolation of β-sitosterol and evaluation of antidiabetic activity of *Aristolochia indica* in alloxan-induced diabetic mice with a reference to in-vitro antioxidant activity. Journal of medicinal plant research, 2012; 6: 1219-1223.

[19]. Goverdhan & Rani, Puchchakayala, Mondi & Thirupathi, Koppula & Rami, S. & Kumar S, Sathesh & Ravi Kumar, Bezwada & Mohan, G.K. Hypoglycemic and antihyperglycemic effect of Aristolochia indica normal and alloxan induced diabetic rats, 2008; 1: 20-29.
[20]. Satheesh Kumar P and Senthil Kumar N. Antihyperglycemic and antihyperlipidemic activities of ethanolic extract of Aristolochia indica roots in streptozotocin-nicotinamide induced diabetic rat, International Journal of Biological & Pharmaceutical Research, 2017; 8(4): 153-158.
[21]. Han J, Xian Z, Zhang Y, Liu J, Liang A. Systematic Overview of Aristolochic Acids: Nephrotoxicity, Carcinogenicity, and Underlying Mechanisms. Front Pharmacol. 2019; 10: 648.
[22]. Cosyns, J. P., Jadoul, M., Squifflet, J. P., De Plaen, J. F., Ferluga, D., and van Ypersele de Strihou, C. Chinese herbs nephropathy: a clue to Balkan endemic nephropathy? Kidney Int. 1994a; 45(6): 1680–1688.
[23]. Cosyns, J. P., Jadoul, M., Squifflet, J. P., Van Cangh, P. J., and van Ypersele de Strihou, C. Urothelial malignancy in nephropathy due to Chinese herbs. Lancet, 1994b; 344(8916): 188.
[24]. Grollman, A. P., Shibutani, S., Moriya, M., Miller, F., Wu, L., Moll, U., et al. Aristolochic acid and the etiology of endemic (Balkan) nephropathy.Proc. Natl. Acad. Sci. U. S. A. 2007; 104(29): 12129–12134.
[25]. Chen, C. H., Dickman, K. G., Huang, C. Y., Moriya, M., Shun, C. T., Tai, H. C., et al. (2013). Aristolochic acid-induced upper tract urothelial carcinoma in Taiwan: clinical characteristics and outcomes. Int. J. Cancer, 2013; 133(1): 14-20.
[26]. Sun, M., Zhang, J., Zheng, C., Liu, Y., Lin, F., Xu, F., et al. Analysis of potential risk factors for cancer incidence in patients with aristolochic acid nephropathy from Wenzhou, China. Ren. Fail., 2015; 37(2): 209-213.
[27]. Chen, C. H., Dickman, K. G., Moriya, M., Zavadil, J., Sidorenko, V. S., Edwards, K. L., et al. Aristolochic acid-associated urothelial cancer in Taiwan. Proc. Natl. Acad. Sci. U. S. A. 2012; 109(21): 8241–8246.
[28]. Rosenquist, T. A., and Grollman, A. P. Mutational signature of aristolochic acid: clue to the recognition of a global disease. DNA Repair, 2016; 44: 205-211.
[29]. Chen, C. J., Yang, Y. H., Lin, M. H., Lee, C. P., Tsan, Y. T., Lai, M. N., et al. Herbal medicine containing aristolochic acid and the risk of hepatocellular carcinoma in patients with hepatitis B virus infection. Int. J. Cancer., 2018.
[30]. Lin, D. C., Mayakonda, A., Dinh, H. Q., Huang, P., Lin, L., Liu, X., et al. Genomic and epigenomic heterogeneity of hepatocellular carcinoma. Cancer Res. 2017; 77(9): 2255–2265.
[31]. Jin K, Su KK, Li T, Zhu XQ, Wang Q, Ge RS, et al. Hepatic Premalignant Alterations Triggered by Human Nephrotoxin Aristolochic Acid I in Canines. Cancer. Prevention Research (Philadelphia), 2016; 9: 324-334.
[32]. Iliopoulos D, Hirsch HA, Struhl K: An Epigenetic Switch Involving NF-KappaB, Lin28, Let-7 MicroRNA, and IL6 Links Inflammation to Cell Transformation. Cell, 2009,139: 693–706.
[33]. Lu ZN, Luo Q, Zhao LN, Shi Y, Wang N, Wang L, et al. The Mutational Features of Aristolochic Acid-Induced Mouse and Human Liver Cancers. Hepatology (Baltimore, Md), 2020; 71: 929–942.
[34]. Faisal, Mohammed, et al. Macro microscopic fingerprints ofpanchanga ofIshwari-*Aristolochia indica Linn.* JPhytopharmacol. 2015: 61-7.