Plant Archives Vol. 21, Supplement 1, 2021 pp. 2636-2640 e-ISSN:2581-6063 (online), ISSN:0972-5210

Plant Archives

Journal homepage: http://www.plantarchives.org
doi link : https://doi.org/10.51470/PLANTARCHIVES.2021.v21.S1.429

REVIEW ARTICLE: PHARMACOGNOSTIC, PHARMACOLOGICAL AND TOXICOLOGICAL REVIEW OF SEEDS OF *HOLARRHENA ANTIDYSENTERICA* (APOCYNACEAE)

Kaur Amrinder and *Kumar Deepak
Department of Ayurveda, School of Pharmaceutical Sciences, Lovely Professional University, Punjab, India
*E-mail: deepak.himsons@gmail.com

ABSTRACT

Holarrhena antidysenterica belongs to the family Apocynaceae is commonly known as kurchi in Hindi, Tellicherry bark in English is a small deciduous tree which is distributed throughout the world and in India, it is found in dry forests. In Indian traditional medicine, *H. Antidysenterica* is popularly used as a medication for dysentery, diarrhoea and intestinal worms. Plant parts such as bark are used to treat anti-microbial, anti-inflammatory, analgesics, amoebiasis, chronic bronchitis, locally for boils, ulcers; The phytochemicals present in the plant include coumarins, ergosterol, flavonoids, phenolic acids, resins, saponins, steroidal alkaloids, tannins, triterpenoids. Pharmacological studies include anti-amnesic, anti-diabetic, antibacterial activity, anti-inflammatory, anti-diarrhoeal, antioxidant/free radical scavenging property, diuretic activity, anti-amoebic, anthelminthic, anti-microbial properties of *Holarrhena antidysenterica.* This review article explored the detailed investigation of the botanical description, phytochemistry and pharmacological actions of *Holarrhena antidysenterica* to afford an objective for further research.

***Keyword*:** *Holarrhena antidysenterica*, Holatosine, Gut motility disorder.

Introduction

India is one of the world's twelve leading biodiversity center with the presence of over 45,000 different plant species, out of this about 15,000-20,000 plants have good medicinal properties of which only about 7,000-7,500 are being used by traditional practitioners. All traditional medicines have their roots in folk medicines and household remedies. 20,000 medicinal plants used in various parts of the world have been identified by WHO. Other figures suggest that the number would range from 35,000 to 70,000 worldwide. It has been estimated by the WHO that 80 % of the world's population relies mostly on conventional medicine. It is recorded in India that 2500 plant species are used by traditional healers and 100 plant species serve as daily sources of medicine. There has been a growing interest in the study of medicinal plants and their common use in various parts of the globe over the last few decades. Traditional medical knowledge of medicinal plants and their use by indigenous cultures is useful not only for the preservation of cultural traditions and biodiversity, but also for the present and future development of community health and drug development. (Korpenwar *et al*., 2011)

Indrayavais a Sanskrit name referring to the seeds of Kuṭaja (*Wrightia antidysenterica*, "Kurchi fruit"), from the Apocynaceae family. The term is used throughout Ayurvedic literature such as the *Carakasaṃhitā*. This synonym was identified by Amarasiṃha in his *Amarakośa* (a Sanskrit botanical thesaurus from the 4th century). The word Indrayava is composed of Indra and *yava* ('seed').

According to the *Mādhavacikitsā* (7th century Ayurvedic work), the plant (Indrayava) is also mentioned as a medicine used for the treatment of all major fevers, as described in the Jvaracikitsā (or "the treatment of fever") chapter. In this work, the plant is also known by the names Kuṭaja, Kaliṅga, Vatsaka and Indrabija

Holarrhena antidysenterica belongs to the Apocynaceae family, commonly known as Kurchi in Hindi, Tellicherry bark in English is a small deciduous tree with white flowers. The plant is distributed throughout the world's tropical and subtropical regions and in India, it is distributed up to 4000 ft altitudes and also found in the dry forest (Sinha *et al*., 2013).

H. Antidysenterica is used for the treatment of atisaara (diarrhoea and dysentery) in the Indian ayurvedic medicine system. The pods have stanyasodhana (a lactodepurant), the indrayava(seeds) have ama and asthapanopaga (adjuncts to enema), according to Charaka, and the plant contains vamaka and arsoghna, which have respectively meticulous and antihemorrhoidal properties. Susruta assigns diuretic properties to the seeds and sukrasodhana (sperm-purifier) to the plant in general. The plant is mentioned in the Susruta Samhita as an antiseptic, vermifuge, febrifuge, detoxicant and is thought to cure malignant ulcers, leprosy, diarrhoea and other virulent skin diseases. The plant is prescribed in modern Ayurveda to treat obesity, asthma, bronchopneumonia, hepatosplenomegaly and rheumatism. *Hollarhena antidysenterica* is a major ingredient in various Ayurvedic preparations used to treat dysentery, diarrhoea,

fever and bacterial infections, such as KutajghanVati, Kutajarista and Kutajachurna (Ali *et al*., 2017).

Description

It is a large deciduous tree, large or small that is 30 to 40 feet tall which yields milky latex. The bark of the stem is greyish-brown and rough. The stem is soft and white. The leaves are simple, large, oval shaped, papery, and smooth or hairy, arranged opposite one another. Its flowers are small, white and arranged in a cluster that resembles a flattened top having colour white and fruits of half inch in size, the petals are shaped like a salver and converge on the right side. Long follicles are the fruits, which look like two slender pencils that come from anode. The follicles have warty white spots on the ground. Dried fruits split open, with brown hair releasing multiple flat seeds (Shah *et al*., 2020).

Compressed, linear or oblong seeds, elongated, margins bent inside, one side convex and the other side concave with longitudinal striation; 1-2 cm long, 0.2-0.3 cm thick, yellowish-brown surface light; odour not distinct; bitter taste.

Taxonomical classification (Gopinath, Thirumal & Kumar, 2020)

Kingdom : Plantae
Subkingdom : Tracheobionta
Super division : Spermatophyta
Division : Magnoliophyta
Class : Magnoliopsida
Subclass : Asteridae
Order : Gentianales
Family : Apocynaceae
Genus : Holarrhena
Species : antidysenterica

Table 1: Vernacular Names of *H. antidysentrica* (Chauhan, 2020)

S.No	Language	Name
1	Sanskrit	BhadraYava, Kalinga, Sakra, Vatsaka
2	Assamese	Dudhkuri
3	Bengali	Kurchi
4	English	Ester Tree, Conessi Seeds
5	Hindi	Indraju, Kurchi, Kuraiya,Indrabija
6	Kannad	KodasigeBeeja
7	Malyalam	Kutakappala
8	Marathi	KudayacheBeej
9	Oriya	Kurej,Keruan
10	Tamil	Kudasapalai
11	Telugu	KodisapalaVittulu, Palakodisa-Vittulu
12	Urdu	Tukhm-e-Kurchi, IndarjaoTalkh

Properties & action: (Bagul *et al*., 2020)

Rasa(taste): Katu(pungent), Tikta(bitter)

Guna(qualities): Laghu(light), Ruksha(dryness)

Virya(potency): Sita(cold)

Vipaka(taste conversion after digestion):Katu(pungent)

Karma(action):Dipana, Sangrahi, Tridoshamaka

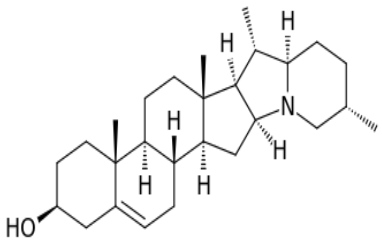
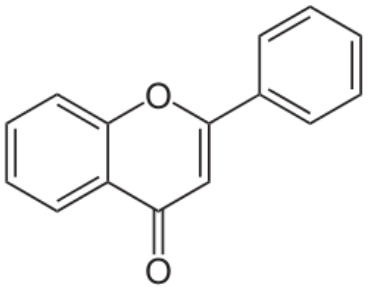
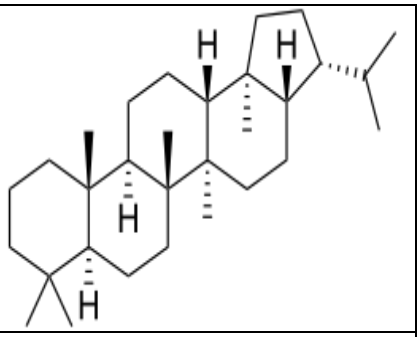
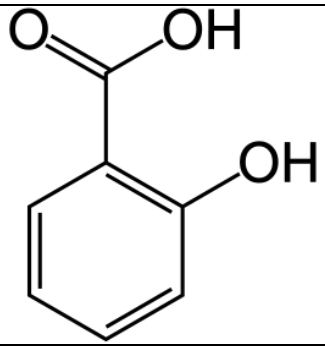
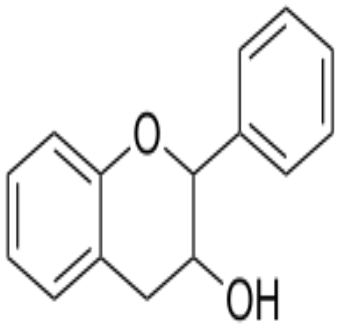
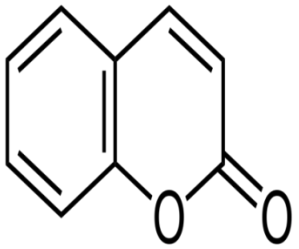
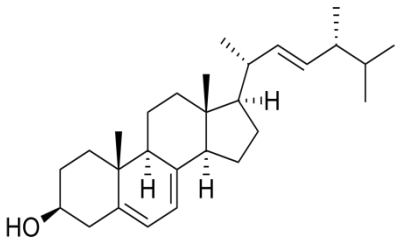
Chemical constituents (Gopinath *et al*., 2020)

Most of the known chemical constituents in *H. antidysentrica* have been found in the stem, bark, leaves and a few in the seeds as well. The major constituents are steroidal alkaloids, flavonoids, triterpenoids, phenolic acids, tannin, resin, coumarins, saponins and ergostenol. The 68 alkaloids which have been discovered from various parts of *H. antidysenterica* to date are listed below in Table 2.

Table 2: Chemical constituents of *H. antidysenterica* (Gopinath, Thirumal& Kumar, 2020)

S.No.	Plant Parts	Constituents
1	Leaf	Holantosine-A ($C_{28}H_{47}NO_6$), Holantosine-B ($C_{28}H_{45}NO_5$), Holantosine-C ($C_{28}H_{47}NO_6$), Holantosine-D ($C_{28}H_{45}NO_5$), Holantosine-E ($C_{28}H_{47}NO_6$), Holantosine-F ($C_{28}H_{45}NO_5$), Holarosine A ($C_{30}H_{47}NO_6$), Holarosine B ($C_{30}H_{47}NO_6$), Holarricine ($C_{21}H_{32}N_2O_3$), Kurchiphyllamine, Kurchaline, Kurchiphylline ($C_{23}H_{47}NO_2$).
2	Stem Bark	Holarrifine($C_{24}H_{38}N_2O_2$), Kurchamide, Kurcholessine, Trimethylconkurchine ($C_{24}H_{38}N_2$), (3),-N-Methylholarrhimine ($C_{22}H_{38}N_2O$), (20),-N-Methylholarrhimine ($C_{22}H_{38}N_2O$), NNN'N′-Tetramethylholarrhimine ($C_{25}H_{44}N_2O$), Conessidine ($C_{21}H_{32}N_2$), Holarrhidine ($C_{21}H_{36}N_2O$), Kurchenine ($C_{21}H_{32}N_2O_2$), Holarrhessimine ($C_{22}H_{36}N_2O$), Holarrhine ($C_{20}H_{38}N_2O_3$), Conkurchinine ($C_{25}H_{36}N_2$), Kurchamine ($C_{22}H_{36}N_2$), 7α-Hydroxyconessine ($C_{24}H_{40}N_2O$), Kurchilidine ($C_{22}H_{31}NO$), Neoconessine (isomer of conessine) ($C_{24}H_{40}N_2$), Holadysenterine ($C_{23}H_{38}N_2O_3$), Kurchessine ($C_{25}H_{44}N_2$), Lettocine ($C_{17}H_{25}NO_2$), Kurchimine ($C_{22}H_{36}N_2$), Holarrhenine ($C_{24}H_{40}N_2O$), Holarrhimine/Kurchicine ($C_{21}H_{36}N_2O$), Holacine ($C_{26}H_{44}N_2O_2$), Holafrine ($C_{29}H_{46}N_2O_2$), Holadysone ($C_{21}H_{28}O_4$), Holacetine ($C_{21}H_{32}N_2O_3$), 3α-Aminoconan-5-ene ($C_{22}H_{36}N_2$), Dihydroisoconessimine ($C_{23}H_{40}N_2$), Conamine ($C_{22}H_{36}N_2$), Conkurchine ($C_{20}H_{32}N_2$),Pubadysone ($C_{21}H_{26}O_3$), Puboestrene ($C_{20}H_{24}O_3$), Pubamide ($C_{21}H_{27}NO_3$),Holadiene ($C_{22}H_{31}NO$), Kurchinidine ($C_{21}H_{29}NO_2$), Kurchinine ($C_{19}H_{24}O_3$),Pubescine ($C_{22}H_{26}N_2O_4$), Norholadiene ($C_{21}H_{29}NO$), Pubescimine ($C_{24}H_{40}N_2O$), Holonamine, Regholarrhenine A ($C_{22}H_{31}NO_2$), Regholarrhenine B ($C_{21}H_{29}NO_2$), Regholarrhenine C ($C_{22}H_{34}N_2$), Regholarrhenine D ($C_{23}H_{38}N_2O$), Regholarrhenine E ($C_{25}H_{44}N_2O_2$), Regholarrhenine F ($C_{25}H_{44}N_2O$).
3	Seed	Conimine ($C_{22}H_{36}N_2$), Antidysentericine ($C_{23}H_{36}N_2O$).

Table 3: Structures of Major Chemical Constituents

		
Steroidal alkaloids	**Flavonoids**	**Triterpenoids**
		
Phenolic acids	**Tannins**	**Coumarins**
		
Ergostenol		

Pharmacological uses

Anti-diabetic activity (Sheikh *et al*., 2013)

The antidiabetic activity of *Holarrhena antidysenterica* seeds extract in streptozotocin-induced-diabetic rats. The experimental protocol designed as animals were divided into six groups (n=6) like normal, diabetic control, Glibenclamide, methanol extract (MEHAD), petroleum ether extract (PEHAD) and aqueous extract (AEHAD). Except normal group other remaining groups were treated with Streptozotocin (STZ) (35 mg/kg body weight) by single i.v. injection to induce diabetes. The diabetic rats were treated with the glibenclamide, MEHAD (250 mg/kg body weight), PEHAD (250 mg/kg body weight) and AEHAD (250 mg/kg body weight) for 18 days. The fasting plasma glucose level, body weight, fasting serum glucose level, serum cholesterol, serum triglyceride, total protein, blood urea, urine glucose and liver glycogen levels were determined. The diabetic rats treated with MEHAD, PEHAD and AEHAD showed significant reduction in fasting serum glucose, serum cholesterol, serum triglyceride, total protein, blood urea, urine glucose and protection from the loss of body weight and increase in liver glycogen content during the treatment period these effects were comparable to those seen in the glibenclamide treated group of rats. This suggests that the *Holarrhena antidysenterica* seed extracts possess antidiabetic activity and further studies are needed to elucidate the mechanism of action and to know the active principles involved in producing the effect.

Antioxidant activity (Ray, 2014)

The water extract and ethanol extract were prepared with the seeds and the antioxidant and phytochemical activities were studied using suitable methods. The free radical scavenging activity was measured using DPPH method. The phytochemicals that were studied included total polyphenol, flavonoids, tannin and ascorbic acid. The ethanol extracts of the seeds were found to show higher results for all the parameters. The ascorbic acid contents were not very high in both the water and the ethanol extract. The seeds of *Holarrhena antidysenterica* have potent antioxidant properties and thus may be used for treatment of diabetes mellitus and several other diseases. Many studies have also been carried out to prove the ability of this plant in the treatment of such diseases.

Diuretic activity (Aslam Khan 2012)

Holarrhena antidysenterica is used as diuretic in traditional medicine. The crude extract of *H. antidysentrica* seeds (Ha.Cr) and its fractions, n-hexane (Ha.Hx), n-butanol (Ha.Bu) and aqueous (Ha.Aq), for their diuretic effect in Wistar rats and to investigate whether the activity is concentrated in any of the fractions. Wistar rats kept on fasting for 24 h with water ad labium, divided into normal, positive control and treated groups were orally given normal saline (20 ml/kg), hydrochlorothiazide (HCT; 10 mg/kg) and different doses of the plant material, respectively. Immediately after dosing, the rats were housed in the metabolic cages. The urine was collected at 2 h interval for 6 h and volume, pH and electrolytes levels were measured. Ha.Cr caused dose-dependent (30 and 100 mg/kg) increase in urine output, indicating the diuretic effect. In addition, Ha.Cr increased urine contents of Na+ and K+, suggesting that the diuretic effect is mediated through increased electrolyte excretion. Similarly, the reference drug, HCT (10 mg/kg), increased urine volume and Na+ and K+ excretion. None of the resultant fractions exhibited diuretic effect comparable to that of the parent crude extract. Ha.Hx was devoid of diuretic effect, Ha.Bu exhibited a mild diuretic effect at 30 mg/kg, whereas, Ha.Aq caused a significant increase in urine output only at 100 mg/kg, indicating that the diuretic activity is distributed among fractions but in an order of increasing polarity of the solvent. The enhanced diuretic effect in the crude extract as compared to any individual fraction is suggestive of the existence of additive and/or synergistic effect in the crude extract. This study shows the presence of diuretic activity in the *H. antidysentrica* possibly mediated through its saluretic effect, which rationalizes its medicinal use as diuretic.

Antibacterial activity (Joice *et al*., 2019)

In the present study of seed and bark of *Hollarhena antidysenterica* was screened for antibacterial activity. Air dried Seed and bark powder of plant was subjected to hot continuous extraction with various solvents like aqueous extracts and acetone extracts. Aqueous extract was prepared by cold maceration. Result: The antimicrobial activity of seed and bark of *Holarrhena antidysenterica* when tested have exhibited different degree of antimicrobial activity against tested organism. So it is found to be effective against all tested microorganisms with inhibition zone ranging from 18- 25mm.

Anti-amoebiasis activity (Shah *et al*., 2019)

Various fraction of *Holarrhena antidysenterica* showed promising activity against the experimental amoebiasis in rats and hamsters. The fruit extract showed anti-protozoal effect against human *Entamoeba histolytica* stain STA, *Trypanosoma evansi*, anticancer effect against human epidrmoid carcinoma of nasopharynx in tissue culture and hypoglycemic activity in rats.

Anti-amnesic activity (Mrinal *et al*., 2018)

Administration of ethanolic extract of *Holarrhena antidysenterica* seeds for 28 days to the separate groups of STZ significantly decrease the level of AChE as compared to the diseased group, prevented the rise in MDA levels and GSH depletion in a dose dependent manners. Cholinergic dysfunction was assessed by acetyl cholinesterase activity. Decreased level of AChE, prevented levels of MDA and Glutathione showed anti amensic property of *Holarrhena antidysenterica*.

Anti-diarrheal activity (Gopinath *et al*., 2020)

When treated with ethanolic extract of seed, castor oil and *E.coli* induced diarrhoea in rats showed an improvement in the density of their dry faeces and suppression of defecation drops.15 Aqueous extract and bark alcoholic extracts were well-known to resist entero invasive *Salmonella enteritidis*, *E. coli* (EIEC), *Shigella boydii*, and *Shigella flexneri*. In rats, diarrhoea was caused by castor oil, a commercially available preparation of *Holarrhena antidysenterica*. The antidysenteric drug kutajaparpativati showed a substantial decrease in watery diarrhoea and small intestine motility. In addition, it showed significant defence of 67.55 percent against castor oil-induced entry polling.

Gut motilitydisorder (Gilani *et al*., 2019)

The pyrilamine-sensitive spasmogenic effect was caused by HaCE at 0.3-10 mg/mL in guinea pig ileum tissues. HaCE (0.01-3.0 mg/mL) triggered mild stimulation when measured in spontaneously contracting rabbit jejunum preparations, accompanied by a relaxant effect at further higher concentrations. The contractile effect was inhibited in the presence of pyrilamine and relaxation was observed at lower concentrations (0.01-0.3 mg/mL). At a concentration range of 0.01-1.0 mg/mL, HaCE prevented the high K+ (80 mM)-induced contractions and shifted the response curves of Ca^{++} concentration to the right, like that triggered by verapamil. Activity-directed fractionation showed that in the aqueous fraction, the spasmogenic component was concentrated, while in the organic fraction, the spasmolytic component was concentrated.

Anticonvulsant activity (Debnath, Dighe, Dighe & Supriya, 2020)

The anticonvulsant activity of ethanolic extract of *Holarrhena antidysenterica* was carried out in swiss albino mice. The anticonvulsant activity of ethanolic extract of seeds of *Holarrhena antidysenterica* (250 and 500 mg/kg, p.o.) in mice was assessed by using maximum electroshock seizure (MES) test, pentylenetetrazol (PTZ), and bicuculine (BC) test. The ethanolic extract of *H. antidysenterica* significantly reduced the duration of seizures induced by maximal electroshock (MES). The ethanol extract in doses of 250 and 500 mg/kg conferred protection (17 and 50%, respectively) on the mice. The same doses also protected animals from tonic seizures induced by Pentylenetetrazol and significantly delayed the onset of tonic seizures produced by Pentylenetetrazol. The extract had no effect on bicuculine induced seizure. The ethanolic extract of *H. antidysenterica* (EEHA) reduced MES, PTZ induced convulsions.

Conclusion

There is tremendous natural drug that have been covered up for decades. *Holarrhena antidysenterica* is a promising medicinal plant with a wide range of pharmacological activities that may, due to its effectiveness and protection, be used in a few therapeutic applications. In general, *H.antidysenterica* has been used to treat diseases such as looseness of the intestines, diarrhoea, anti-oxidant and anti-diabetic activity. This plant contains unidentified chemical constituents that are useful for the synthesis and

formulation of novel drugs for various infections by pharmacists.

References

Ali, K.M.; Ghosh, D.; Chatterjee, K.; Ghosh, A.M. (2017). Bio-efficacy study of aqueous extract of *Holarrhena antidysenterica* seed on hyperglycemia and oxidative stress in streptozotocin-induced diabetic rats, JAST, Vol-3.

Aslam Khan. (2012). An in vivo study on the diuretic activity of *Holarrhena antidysenterica*. *African Journal of Pharmacy And Pharmacology*, *6*(7). doi: 10.5897/ ajpp11.395

Bagul, D.; Bagul, D.; MD(Ayu), D.; manyengawana, MD(Ayu), D.; & MD(Ayu), D. *et al*. (2020). Kutaja – Benefits, Usage, Dose, Side Effects – Ayurveda Details. Retrieved 22 November 2020, from https://www. easyayurveda.com/2013/10/17/kutaja-benefits-usage-dose-side-effects-ayurveda-details/

Chauhan, D. (2020). Kutaja, Kurchi (*Holarrhena antidysenterica*) - Properties, Benefits & Dosage. Retrieved 22 November 2020, from https://www. planetayurveda.com/library/kutaja-holarrhena-anti dysenterica/

Debnath, J.; Dighe, S.; Dighe, N. and Supriya, M. (2020). An Experimental Evaluation of Anticonvulsant Activity of Ethanolic Extract of Seeds of *Holarrhena antidysenterica* In Mice. Retrieved 22 November 2020, from https://rjppd.org/AbstractView.aspx?PID=2011-3-1-20

Gopinath, G.; Thirumal, M. (2020). *Holarrhena antidysenterica* Linn. – A Review, Research Journal of Pharmacy and Technology, Vol.13

Gilani, A.; Khan, A.; Khan, A.; Bashir, S.; Rehman, N.; &Mandukhail, S. (2010). Pharmacological basis for the medicinal use of *Holarrhena antidysenterica* in gut motility disorders. *Pharmaceutical Biology*, *48*(11): 1240-1246.

Joice, M.; Kumaran, E. (2019). Antibacterial activity of seed and bark extracts of *Holarrhena antidysenterica*, Natural Products-An Indian journal, Vol. 5

Korpenwar, A.N. (2011). Traditional Medicinal Plant *Holarrhena antisenterica* (L.) Wall. Ex A. DC. In the Treatment of Diabetes: International Journal of Recent Trends in Science And Technology, 1: 120-123.

Mrinal, S.N. (2018). A Review on Pharmacological Aspects of *Holarrhena antidysenterica*, Scholars Academic Journal of Pharmacy.

Ray, A. (2014), Evaluation of the Antioxidant Activities of the Seeds of *Holarrhena antidysenterica* grown in West Bengal, India, International journal of current microbiology and applied Sciences, 3: 562-568.

Sinha, S.; Sharma, A.; Reddy, P.; Rathi, B.; Prasad, N. and Vashishtha, A. (2013). Evaluation of phytochemical and pharmacological aspects of *Holarrhena antidysenterica* (Wall.): A comprehensive review. Journal of Pharmacy Research, 6(4): 488-492.

Shah, S.; Usmanghani, K.; Akhtar, N.; Asif, H.; Akram, M. and Ahmed, K. *et al*. (2020). Monograph of *Holarrhena antidysenterica* (linn.) Wall. Retrieved 22 November 2020, from https://www.arjournals.org/index. php/ ijpm/article/view/129/121

Sheikh, Y.; Manral, M.; Kathait, V.; Prasar, B.; Kumar, R. (2013). Computation of In Vivo Antidiabetic Activity of *Holarrhena antidysenterica* Seeds Extracts in Streptozotocin-Induced-Diabetic Rats, UK Journal of Pharmaceutical and Biosciences,Vol. 1(1)