



## PLUMBAGO ZEYLINICA A POTENT HERB FOR VARIOUS AILMENTS: A REVIEW

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### ABSTRACT

*Plumbago zeylinica* belongs to family Plumbaginaceae. Its common name is Chitrak. *Plumbago zeylinica* have many activities like anticancer, anti-inflammatory, antioxidant, antibacterial, antifungal. Its chemical constituents are Plumbagin, 2-(2,4 Dihydroxy-phenyl)-3, 6, 8- trihydroxy-chromen-4-one, 3, 3-Biplumbagin, Chittanone, Isozeylenone, Maritinone, Elliptone, Droserone in which Plumbagin gives very potent effect.

**Keywords:** *Plumbago zeylinica*, Chitrak, Antioxidant, Antimicrobial, Anticancer activity, Plumbagin.

### INTRODUCTION

*Plumbago zeylinica* is an age old Rasayan herb in traditional Ayurved. It belongs to family Plumbaginaceae. *Plumbago zeylanica* Linn. is distributed as a weed throughout the tropical and subtropical countries of the world<sup>1</sup> native to south asia and cultivated throughout India and srilanka.<sup>1-8</sup>

#### Common names

**English:** White leadwort, Ceylon leadwort, plumbago<sup>9-12</sup>

**German:** Bleiwurz, Zahnkraut.<sup>9-14</sup>

**India:** Chitrak, chitramol<sup>9-12</sup> Chira, Chitra, Chitrakmula<sup>15</sup> Chitrakmula, Bilichitrama<sup>15</sup>, Vellakeduveli<sup>15</sup>, Chitra Bengali: Chita<sup>15</sup>, Kodiveli, Chitramoolam<sup>15</sup>, Chitramulam.<sup>15</sup>



Plants of *Plumbago zeylanica*

### CLASSIFICATION

|               |                  |
|---------------|------------------|
| Kingdom       | : plantae        |
| Subkingdom    | : Tracheobionta  |
| Superdivision | : Spermatophyta  |
| Division      | : Magnoliophyta  |
| Class         | : Magnoliopsida  |
| Subclass      | : Caryophyllidae |
| Order         | : Caryophyllales |
| Family        | : Plumbaginaceae |
| Genus         | : Plumbago       |
| Species       | : Zeylanica      |

### BOTANICAL DESCRIPTION

**Stem:** Stems are spreading, branched, diffused, erect, suberect, striate, glabrous, green somewhat woody, 1-3 mtr long.<sup>16-18</sup>

**Leaves:** Leaves are thin, 3.8-7.5 by 2.2-3.8 cm, alternate, light to dark green, ovate or oblong in shape, subacute, entire, glabrous, shortly and abruptly attenuated into a short petiole; petiole narrow, amplexicaul at the base and are often dilated into stipule like auricles.<sup>16,17</sup>

**Flower:** Flowers are white in colour terminal, bisexual; rachis glandular; bracteoles.<sup>14</sup> Ovate, acuminate, often borne in elongated branched spikes.<sup>16-18</sup>

**Calyx:** Calyx are white with 5 lobes, lobes ovate to lanceolate, 1-1.2 cm, tubular densely covered with stalked, sticky glands.<sup>17</sup>

**Corolla:** Corolla are tubular, slender, white, 1-1.3 cm long, tubular, resistant, densely covered with stalked glands.<sup>19</sup>

**Stamen:** Stamen unilocular, 5 in number, free from corolla.<sup>17</sup>

**Stigma:** 5 forked, ovary superior.<sup>17</sup>

**Capsule:** Oblong, pointed enclosed in persistent viscid calyx, pale yellow to brown in colour.<sup>14,15</sup>

**Seeds:** Seeds are cylindrical flat and dark brown in colour.<sup>16</sup>

**Flowering time:** *Plumbago zeylanica* blooms round the year except winter.<sup>21</sup>

**Roots:** Roots are reddish to deep brown in colour and have disagreeable odour. About 30 cm in diameter scars of rootlets are also present.<sup>17</sup>

### USES

*Plumbago zeylanica* has been used for hundreds of years as a traditional system of medicine.<sup>1</sup> It possesses activities like analgesic, antibacterial, antifungal, memory-inducing, anti-cancer, anti-inflammatory, hepatoprotective, larvicidal, anti-diabetic, anti-fertility, and immunosuppressive. The roots of *P. zeylanica* are also used as expectorant, antirheumatic, anti-scabies, appetite stimulant, anti-diarrhoeal, anti-periodic, anti-malarial and for the treatment of leprosy.<sup>1</sup> The whole plant, the roots, and powder of the roots<sup>13,14</sup> used in fever and malaria, against diarrhoea, dyspepsia, piles, and skin diseases including leprotic lesions<sup>10</sup>, in Nepal it is used as an antiviral medicine, in Taiwanese it is used folk medicine for anti *Helicobacter* activity, in Assam it is used for family planning and birth control and permanent sterilization, treatment of gastro-intestinal complaints<sup>22</sup> against parasitic diseases, scabies and ulcers<sup>23</sup>. Amrita Bindu, a salt-spice-herbal mixture, is used as an antioxidant<sup>14</sup>. Tincture of root bark is used as an antipatriotic. It acts as a powerful sudorific. Leaves are caustic, vesicant aphrodisiac and good for scabies.<sup>24</sup>

### CHEMICAL CONSTITUENTS

The preliminary phytochemical screening in petroleum ether, ethanol and aqueous extracts of stem and leaves of *Plumbago zeylanica* revealed the presence of alkaloids, carbohydrates, triterpenoids, flavonoids, gum, mucilage, protein, fatty acids and saponine.<sup>24-29</sup>

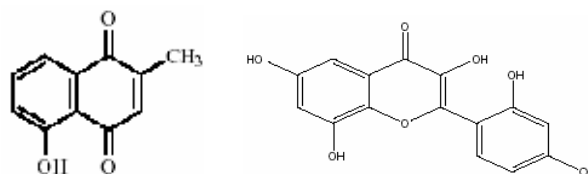
**Crude extracts:** alkaloids, phenols and flavonoids<sup>13</sup>

**Roots:** The naphthoquinones plumbagin, composed naphthoquinones, like plumbagin, 3-biplumbagin, chloroplumbagin, chitanone, elliptone. The coumarins seselin, 5-methoxyseselin, suberosin and xanthyletin. Other compounds were 2,2-dimethyl-5-hydroxy-6-acetylchromene, plumbagin acid,  $\beta$ -sitosterol,  $\beta$ -sitosteryl-glucoside, bakuchiol, 12-hydroxyisobakuchiol, saponaretin, isoorientin, isoaffinetin, psorealen. Between all these compounds plumbagin is the major ingredient (5-hydroxy-2-methyl-1,4-naphthoquinone, (C<sub>11</sub>H<sub>8</sub>O<sub>3</sub>)).<sup>13, 30,31</sup>

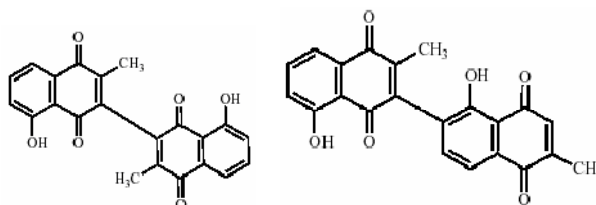
**Flower:** Flowers contain plumbagin, zeylanone, and glucose.<sup>32,33</sup>

**Leaves:** Leaves contain plumbagin, chitanone.<sup>32,33</sup>

**Stem:** Stem contain plumbagin, zeylanone, isozeylanone, sitosterol, stigmasterol, campesterol, and dihydroflavinol-plumbaginol.<sup>32,33</sup>

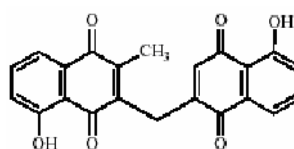


Plumbagin 2-(2,4-Dihydroxy-phenyl)-3,6,8-trihydroxy-chromen-4-one



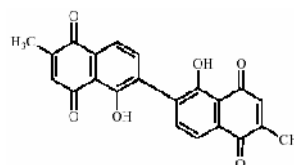
3,3-Biplumbagin

Chittanone

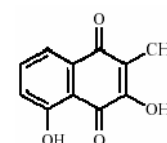


Isozeylanone

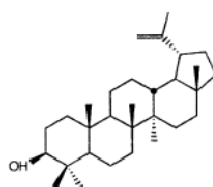
Maritnone



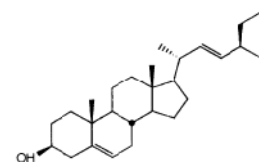
Elliptone



Droserone



Lupeol



Stigmasterol

To identify the phytochemical components present in the ethanolic root extract of the plant by phytochemical screening methods and GC-MS analysis. The phytochemical screening showed the presence of alkaloids, tannins, steroids, flavonoids, saponins, anthraquinones, cardiac-glycosides, phlobatinnins and carbohydrates. The gas chromatography-mass spectrometry (GC-MS) analysis also identified the presence of phytochemical components like phenolics (Phenol, 2,4-bis(1,1-dimethylethyl) (RT: 6.796), Cyclopentadecane (RT: 7.305), fatty acids/methyl esters, Ferropfen (RT: 9.602), 1,1,1,5,7,7,7-Heptamethyl-3,3-bis(trimethylsiloxy)tetrasiloxane (RT: 8.253), Indazol-4-one, 3,6,6-trimethyl-1-phthalazin-1-yl-1,5,6,7-tetrahydro- (RT: 10.162), 2H-Indol-2-one,1-(2,6-dichlorophenyl)-1,3-dihydro- (RT: 11.191), 2-Methyl-7-phenylindole (RT: 14.540), 1H-Indole-2-carboxylic acid, 6-(4-ethoxyphenyl)-3-methyl-4,5,6,7-tetrahydro-, isopropyl ester (11.528), and Anthranilic acid, 3-chloro-N-(o-chlorophenyl)- (RT:12.443).<sup>34</sup>

To investigate the chemical constituents from the aerial parts of *Plumbago zeylanica* L. The chemical constituents were isolated by various column chromatographic methods and the structures were elucidated by various spectroscopic methods, especially 2DNMR spectra. A new triterpenoid,  $1\beta,3\beta,11\alpha$ -trihydroxy-urs-12-ene, together with six known compounds, androsta-1,4-diene-3,17-dione, isoshinanolone, neoehinulin A, harman, ergostadiene- $3\beta,5\alpha,6\beta$ -triol<sup>35</sup> and *N*-(*N'*-benzoyl-*S*-phenylalaninyl)-*S*-phenyl alaninol were isolated from the aerial parts of *P. zeylanica*.<sup>36</sup>

In order to find out the better technique for plumbagin extraction, were applied: static maceration, dynamic maceration, with assistance of ultrasonic waves and in Soxhlet apparatus. Four compounds were qualitatively detected in all extracts: the naphthoquinones plumbagin and *epi*-isoshinanolone, palmitic acid and sitosterol. Plumbagin was always the major component in all analyzed extracts and it was quantitatively determined by gas chromatograph coupled with mass spectrometer. Soxhlet was the most efficient extraction technique however, prolonged heating time promoted plumbagin degradation.<sup>37</sup>

#### Activity of chemical constituents

##### Plumbagin as a reference compound

The root being a vital component in these formulations, its quality and consistency is of prime importance. Plumbagin being the major bioactive chemical was used as a reference standard with which the HPTLC chromatogram obtained for each sample was compared. Plumbagin present in each sample was quantified using a calibration graph of the reference standard. The study of the presence of any variation in the plumbagin content due to change in season and storage. Sufficient quantities of root was collected during the month of July 2008 and stored at room temperature for the assay of Plumbagin. From August onwards every month, fresh root samples were also collected till June 2009. Simultaneous comparison of the fingerprints of n-hexane extract of the roots as well as estimation of plumbagin was done on the samples collected and the stored sample at room temperature using HPTLC technique. The plumbagin content showed a sharp decline from July 2008 to June 2009 on the stored root samples. The study established more concentration of Plumbagin constituent in February followed by January. The content was found to be very less in April. Hence the root may show more efficacy if collected in February. The technique is simple and cost effective.<sup>38</sup>

##### Antioxidant activity

A new flavonoid 2-(2, 4 Dihydroxy-phenyl)-3, 6, 8-trihydroxy-chromen-4-one isolated from the roots of *Plumbago zeylanica* and determined the antioxidant activity by free radical scavenging and superoxide radical scavenging assays. They revealed the significant antioxidant activity of the roots extract as compared to

standard flavonoid (quercetin). The antioxidant activity by DPPH and by NBT were greater than that of standard.<sup>39</sup>

##### Anticancer and Antibacterial activity

Plumbagin, a naphthoquinone from the roots of *Plumbago zeylanica* is known to possess anticancer and antibacterial activity. In this study revealed the mitochondrial pathway involved in plumbagin-induced apoptosis. We also found that the generation of ROS was a critical mediator in plumbagin-induced apoptosis, which would be abrogated completely by antioxidant, NAC. The anticancer effect of plumbagin was investigated in vivo using NB4 tumor xenograft in NOD/SCID mice. The incidence of formation, growth characteristics, body weight and volume of tumors were observed. The histopathologic examination of tumors and organs were made. The results showed that intraperitoneal injection of plumbagin (2 mg/kg body weight) daily for 3 weeks resulted to a 64.49% reduction of tumor volume compared with the control. Furthermore, there was no overt manifestation of toxicity such as weight loss, tissue damage and behavior change which appeared in Doxorubicin-treated mice (1 mg/kg thrice a week). These results indicate that plumbagin has potential as a novel therapeutic agent for myeloid leukemia.<sup>40</sup>

#### PHARMACOLOGICAL ACTIVITY

##### Anticancer activity

The methanolic extracts of *P. zeylanica* was evaluated for antiproliferative activity against Ehrlich Ascites Carcinoma cells (EAC) in swiss albino mice at dose 20,30 and 40 mg/kg /day by Intraperitoneal. The extract was administered intraperitoneally for 14 days by same dose and animal. Bleomycin was used as a positive control. The result was that the methanolic extracts have strong antiproliferative activity.<sup>41</sup>

##### Wound healing activity

*Plumbago zeylanica* is used in a herbal composition with combination of *Rubia cordifolia*, *Centella asiatica*, *Terminalia bellerica*, *Withania somnifera* to evaluate wound healing activity in albino rats. Wound healing activity of the plant was evaluated by formulating the drug in ointment dosage form and then compared with a marketed formulation (Soframycin cream) as reference drug. The herbal drug combination has been observed to promote healing of wounds in animals.<sup>42,43</sup>

##### Anti oxidant activity

The antioxidant activity and radical scavenging activity of methanolic extracts of selected plant materials, traditionally used by the tribes of Attapady regions as folk remedies was evaluated against 1, 1-diphenyl-2-picrylhydrazyl (DPPH) free radical. *Cassia occidentalis*, *Clitoria ternatea*, *Trianthema decandra*, *Capparis zeylanica*, *Anisomeles malabarica* and *Plumbago zeylanica* exhibited strong antioxidant activity as compared to other plants. *Trianthema decandra* showed the highest antioxidant activity. The study SHOWS that





these plants are of therapeutic potential due to their high free radical scavenging activity.<sup>44</sup>

### Antimicrobial activity

Petroleum ether, ethanol and aqueous extract of leaves and stems of *Plumbago zeylanica* were investigated against bacteria and fungi by paper disc method. Gentamycin and Amphotericin-B were used as a standard drug respectively. The maximum activity was observed in ethanol extract against *Micrococcus luteus* (12mm) and minimum activity was observed in pet-ether extract against *Staphylococcus aureus* and *Micrococcus luteus* at inhibition range was observed (7mm). The result suggest ethanol and petroleum ether extract showed moderate anti-bacterial activity and aqueous extract did not active against negative bacterial species. In antifungal, it was found that among the extracts and compare with standard, ethanol extract showed a significant anti-fungal activity.<sup>25</sup>

This work assesses the antibacterial activity of plumbagin (5-hydroxy-2-methylnaphthalene- 1,4-dione) and of methanol, chloroform and aqueous extracts of *Plumbago zeylanica* L. root against various pathogenic bacteria, and the minimum inhibitory concentrations (MICs). Plumbagin and chloroform extracts of *Plumbago zeylanica* L. root showed antibacterial activity against *Escherichia coli*, *Salmonella typhi* and *Staphylococcus aureus*. Inhibition against *Klebsiella pneumoniae*, *Serratia marcescens* and *Bacillus subtilis* was moderate, and lower against *Proteus vulgaris* and *Pseudomonas aeruginosa*. The methanolic extract exhibited moderate activity and the aqueous extract weak activity against the bacterial strains as assessed by disc diffusion assays. The bioactive compound plumbagin and extract of *Plumbago zeylanica* root show a wide spectrum of antibacterial activity. The compound shows promise as a new drug for various bacterial infectious diseases.<sup>45</sup>

Antibacterial activity of methanolic and chloroform extracts from the *Plumbago zeylanica* were carried out against five different organism of *Streptococcus aureus*, *Staphylococcus aureus*, *Bacillus*, *Pseudomonas aeruginosa*, *E.coli* using disc diffusion method. Both the extracts showed antibacterial activity against most tested bacteria. The methanolic extracts were more active against the entire tested organism.<sup>46</sup>

The antimicrobial effect of *Plumbago zeylanica* Linn.leaf extract was evaluated on microbial strains like gram positive species *Staphylococcus aureus*, and *Bacillus subtilis* and gram negative species *Escherichia coli* and *Pseudomonas aeruginosa*. The solvent used for extraction of plant were petroleum ether, chloroform and alcohol. The alcoholic extract of leaves of *Plumbago zeylanica* shows maximum antimicrobial activity. The in vitro antimicrobial evaluation was carried out by agar disc diffusion method. The significant antibacterial activity of active extract was compared with standard antibiotic Ampicillin. The samples of leaves were further used for the phytochemical studies. Results of the phytochemical

analysis indicated the presence of alkaloids, glycoside, reducing sugars, simple phenolics, tannins, Lignin, saponins and flavonoids. The antibacterial activities of the leaves were due to the presence of various secondary metabolites.<sup>47</sup>

Secondary metabolites from medicinal plants are associated with toxic hormonal antineoplastic effects. The study is focused on comparative antimicrobial effect and phytochemical screening of *Plumbago zeylanica*, *Ocimum gratissimum*, *Bryophyllum fedtschenkoi*. These medicinal plants were subjected to antimicrobial and phytochemical screening. The extraction was taken from these plants using the solvents ethanol, benzene and aqueous. The ethanolic extracts of plant leaves showed significant activity against bacterial and fungal pathogen and results were unpored with standard antibiotics such as *Ampecillin*, *Penicillin* *Streptomycin* *Griscofulenin*, *anpolenicin* and *flunonazole*. The phytochemical component were identified by using thin layer chromatographic and the results further technique and the results further technique supported that some Indian medicinal plants possess. Potential antimicrobial compounds which will be used cure most of the diseases.<sup>48</sup>

### Hepatoprotective activity

Petroleum ether extract of root of *Plumbago zeylanica* was investigated for hepatoprotective activity against paracetamol induced liver damage. Various biochemical parameters were studied to evaluate the hepatoprotective activity of ethanolic extract. In serum total bilirubin, total protein, aspartate transaminase, alanine transaminase, alkaline phosphatase, lactate dehydrogenase, total Cholesterol and serum triglycerides were determined to assess the effect of the extract on the paracetamol induced hepatic damage. The study was also supported by histopathology of liver sections. Results of this study revealed that the markers in the animals treated with paracetamol recorded elevated concentration indicating severe hepatic damage by paracetamol, whereas the blood samples from the animals treated with petroleum ether extract of roots showed significant reduction in the serum markers indicating the effect of the plant extract in restoring the normal functional ability of the hepatocytes. The dosage of extract of plant roots used was 300 mg/kg bodyweight of rat. The petroleum ether root extract of *Plumbago zeylanica* could afford a significant protection against paracetamol induced hepatocellular injury.<sup>49</sup>

The hepatoprotective activity of methanolic extract of aerial parts of *Plumbago zeylanica* in CCl<sub>4</sub>-induced hepatotoxicity in wistar rats. Silymarin (100mg/kg, p.o.) was given as reference drug. The extract of aerial parts of *Plumbago zeylanica* have shown very significant hepatoprotection against CCl<sub>4</sub>-induced hepatotoxicity in wistar rats by reducing serum total bilirubin, SGPT, SGOT and ALP levels. Histopathological studies also confirmed the hepatoprotective nature of the extract.<sup>50</sup>



### Antidiabetic activity

Alpha-glucosidase inhibitory activity of fifteen Indian medicinal plants has been evaluated by *in vitro* enzyme assay. Methanol extracts of *Cyperus rotundus* (tubers), *Plumbago zeylanica* (root), *Symplocos racemosa* (bark), and *Terminalia arjuna* (bark) had displayed 100% inhibition with the IC<sub>50</sub> value of 3.98 µg/ml, 3.46 µg/ml, 8.16 µg/ml and 0.69 µg/ml, respectively. Bark extract of *Terminalia arjuna* is highly effective against alpha-glucosidase activity even at nanogram concentration. Plant parts of *Piper retrofractum* (stem), *Zingiber officinale* (rhizome), *Acorus calamus* (rhizome), *Picrorhiza kurroa* (rhizome), *Marsdenia tenacissima* (stem), *Clerodendron serratum* (root), and *Rubia cordifolia* (root) are not effective and they require high concentration to exhibit inhibition. Potential plants that show maximum inhibition at low concentration (<10 µg/ml) were subjected to kinetic analysis to determine the mode of inhibition of the enzyme. *Cyperus rotundus*, *Symplocos racemosa* and *Terminalia arjuna* exhibited uncompetitive inhibition and *Plumbago zeylanica* had displayed mixed inhibition to alpha-glucosidase enzyme activity. From the enzyme assay, we infer that *Cyperus rotundus*, *Plumbago zeylanica*, *Symplocos racemosa* and *Terminalia arjuna* contain potential alpha-glucosidase inhibitors that can be exploited for its use in the treatment of diabetes.<sup>51</sup>

### Behavioral activity

Evaluated the effect of the chloroform extract of *Plumbago zeylanica* roots on learning and memory of mice in scopolamine induced amnesia. The extract significantly reversed the amnesia induced by scopolamine at the dose as low as 0.4mg/kg i.p. Furthermore, the authors found that the *Plumbago zeylanica* at dose 200mg/kg showed promising memory enhancing effect in mice.<sup>56</sup>

### Antisickle-cell activity

The roots of *Plumbago zeylanica* (Plumbaginaceae) and *Uvaria chamae* (Annonaceae) have been used in folklore medicine in the management of sickle-cell disease (SCD) in South-West Nigeria. Using both crude methanol extract and its aqueous fraction, *in vitro* antisickling activities of these plant parts were evaluated using p-hydroxybenzoic acid and normal saline as positive and negative controls, respectively. Phytochemical screening of the investigated plant specimens revealed the presence of flavonoids, saponins, alkaloids, tannins, cardiac glycosides free and combined anthraquinones. Extracts/fractions of *P. zeylanica* had a significantly higher ( $p < 0.05$ ) antisickling activity at the tested concentrations of 10.0, 1.0 and 0.1 mg/ml. Therefore, the use of these plants by the traditional medical practitioners in the treatment of SCD in Ogun State, Nigeria is justified. The implication of these results is in defining the role of each plant specimen in traditional recipes for SCD management and drug development is presented.<sup>53</sup>

### Anticonvulsant activity

The anticonvulsant activity of *Plumbago zeylanica* Linn. leaf extract in pentylene tetrazole and maximum electroshock induced convulsion. Result concluded that the doses of extract did not protect the animals from pentylene tetrazole and maximum electric shock induced convulsion the entire animals showed convulsion. The extract also did not delay the onset of convulsions in pentylene tetrazole induced convulsions. The authors clearly stated that extract did not show any anticonvulsant activity.<sup>54</sup>

### Anti-inflammatory activity

Studied the anti-inflammatory and cytotoxic effects of the methanolic and dichloromethane extracts of root of *Plumbago zeylanica* respectively. The methanolic extracts produced good inhibition of acute inflammation in Carrageenin induced raw paw oedema. The lethal concentration (LC50) value was observed for crude dichloromethane extract and its components betasitosterol and guggultetrol-18-ferrulate and it was found to be 90, 75 and 65 ppm, respectively. The authors ascertained and proved the anti-inflammatory and cytotoxic effects of the plant.<sup>54</sup>

### Anti-implantation activity

The anti-implantation activity of hydroalcoholic extract of *Plumbago zeylanica* Linn leaves in adult female wistar rats, and found that the extract had very significant antiimplantation activity in dose dependent manner, at 100 mg/kg and 200 mg/kg extract showed 58.03% and 95.16% antiimplantation activity, respectively. Result concluded the significant anti-implantation activity of the extract.<sup>55</sup>

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