

## A REVIEW ON PLUMBAGO ZEYLANICA LINN. : AS AN ANTIFERTILITY AGENT

Nirali Chhodavadiya<sup>1\*</sup>, Ms. Krupa Vyas<sup>2</sup>, Dr. Pragnesh Patani<sup>3</sup>

<sup>1\*,2,3</sup>Khyati College of Pharmacy, Palodia, Ahmedabad

**\*Corresponding Author:** Nirali Chhodavadiya

\*Khyati College of Pharmacy, Palodia, Ahmedabad, Email: niralichhodavadiya@gmail.com

### Abstract:

The plant species *Plumbago zeylanica*, also known as "Lead wort-white," is a multifunctional herb with a chromosomal number of 24. It is found in the subtropics and tropics and is used as a starter, diuretic, expectorant, and for treating various conditions such as piles, diarrhoea, dysentery, and peptic ulcers also prevent fertility. The leaves of this plant are consumed by locals in Malaya to induce abortion. Oestrogenic chemicals are present in the human diet, leading to discussions on how they can modulate a range of dysfunctions and illnesses influenced by hormones. Since the beginning of written history, people have been looking for an oral contraceptive that would limit human fertility. Despite the wide range of synthetic contraceptives agents available, they cannot be continuously employed due to their adverse effects. In folklore Indian medicine, numerous native medications have been mentioned for the treatment of various reproduction-related conditions. Plumbagin contained in the roots of this plant is responsible for antifertility and uterine action, according to a literature review. In this study, the stems of *P. rosea* were assessed for potential antifertility effects. If the medication was found to be effective, the removal of this avoiding the use of an abortion-inducing plant would be beneficial. In Europe today, the pill is one of the most frequently used methods of birth control, with 19.1% of women between the ages of 15 and 49 taking it on average. Since the introduction of three new generations of oral contraceptives that work together (COCs) in 1960, it has become necessary to use only selected, physiologically active botanical compounds that act as fertility-regulating agents safe and not disrupt the regular cycles of reproduction.

**Keywords:** Anti-fertility agent, *Plumbago Zeylanica*, Estrous cycle, abortifacient, Antiovolatory activity, medicinal properties

### [1] INTRODUCTION

The plant species *Plumbago zeylanica*, often known by its trade or common names as "Lead wort-white," is also known in vernacular as Chitraka, Kodiveli, Chitramulamu, Tellachitramulamu, Agnichela, and Agnimaala. The family includes "Ceylon Leadwort" and "Flowered." Plumbaginaceae. The source taxon is present everywhere as a weed. It is well known that the root is both abortifacient and possess vesicant qualities. It is utilized as a starter, diuretic, expectorant, with piles, diarrhoea, dysentery, and peptic ulcers. For filarial leg, the root paste is used topically. When applied topically. For early maturation, abscess rupture, and healing. The source powder taken orally with honey decreases inflammation hypercholesterolemia and promotes the production of

blood.<sup>1</sup>The multifunctional herb *Plumbago zeylanica* L., sometimes known as *P. viscosa* Blanco, has chromosomal number  $2n=24$ . South Asian by birth, the species is dispersed across the majority of the subtropics and tropics. The sap of *P. zeylanica* discolours the skin in a manner reminiscent of lead, which accounts for its both the common name Plumbago and its Latin name leadwort.<sup>2</sup> The leaves of this plant are consumed by locals in Malaya to induce abortion. Oestrogenic chemicals are present in the human diet, which has led to intriguing discussions on how they can modulate a range of dysfunctions and illnesses influenced by hormones. Since the beginning of written history, people have been looking for an oral contraceptive that would limit human fertility. Despite the wide range of synthetic contraceptives agents are available, however they cannot be continuously employed because repercussions (Vaidya et al., 2006). In folklore Indian medicine, numerous native medications have been mentioned for the treatment of various reproduction-related conditions. Numerous plant preparations are said to have antifertility properties, regulation properties, but few have been put to the test. The plumbagin contained in the roots of this plant is responsible for antifertility and uterine action, according to a literature review (Ravikanth & Prakash, 2010). In our investigation of phytochemicals, it was discovered that Plumbagin is also present in the stems. In this regard, our goal was to assess the stems of *P. rosea*'s potential antifertility effects. If the medication was found to be efficient, the removal of this avoiding the use of an abortion-inducing plant.<sup>3</sup> Today's synthetic contraceptives include serious adverse effects such hormonal imbalance, hypertension, an increased risk of cancer, and weight gain. Consequently, there is a critical need to replace these substances offer a secure and efficient replacement, such as plant-base hormonal contraceptives.<sup>4</sup> In Europe today, the pill is one of the methods of birth control that is most frequently used; 19.1% of women between the ages of 15 and 49 take it on average. According to reports, the use of birth control pills is widespread. Among Northern and Western Europe's highest lowest in Eastern and Western (25.6%, 31.5%) Europe's south (11.0%, 15.8%). Since their introduction in 1960, There are three new generations of oral contraceptives that work together (COCs) have been authorized, varying in their ratio of synthetic estrogens and Progestins, or progesterones (As stated by Khialani and co.4).The most often prescribed COCs in 2016 were those containing the progestins, levonorgestrel, norethisterone, or norgestimate. The UK, the Netherlands, and Denmark. In German COCs of the fourth generation contain currently, the progestin dienogestare are the usually recommended COCs.<sup>5</sup> India is home to a number of medicinal herbs with long-standing antifertility properties. These plants prevent females from getting pregnant by functioning as (a) Estrous Cycle disruptors (a), anti-estrogenic substances (b), anti-implantation substances (c), or abortifacient substances. For the benefit of reader' Because of the serious resource depletion caused by the world's population growth, humankind has been obliged to create new techniques for controlling reproduction. Although there has been significant improvement in the creation of fertility-controlling technologies however, the majority of current approaches use chemicals. Formulations with negative effects due to not being herbal effects. Consequently, it has become necessary to utilize only selected, physiologically active botanicals compounds that act as fertility-regulating agents safe and not disrupt the regular cycles of reproductions convenience. And the following categories describe antifertility plants like, *Rivea hypocrateriformis*, *Momordica charantia*, *Anethum graveolens*, *Plumbago zeylanica*, *Citrus medica*, *Azadirachta indica*, *Curcuma longa* etc.<sup>6</sup>



Figure 1: *Rivea hypocrateriformis*



Figure 2: *Momordica charantia*



Figure 3: *Anethum graveolens*



Figure 4: *Plumbago zeylanica*



Figure 5: *Citrus medica*



Figure 6: *Azadirachta indica*



**Figure 7: *Curcuma longa***

The length of sexual contact, the frequency of coitus, and the age of the couple all affect the likelihood of conception. After one month of unprotected sexual activity, the average young couple has a 25% chance of being pregnant; after six months, 70% of the couples become pregnant. And 90% of couples have a 90% chance of getting pregnant within a year. 5% of the couples only will become pregnant in one and a half to two years. The causes are equally the fault of both men and women. The majority of infertile Couples are affected by one of these three main factors, such as a male factor or ovulatory illness, or tubal-peritoneal dysfunction. According to literature, vaginismus and Females between the ages of 20 and 24 tend to have increased dyspareunia.<sup>7</sup> Male rats and mice have been used to evaluate the antifertility effects of numerous native plants. Plants have offered a source of ideas for new medication molecules, as herbal medications have gained popularity contributions to enhancing human health and happiness Plants have been utilized all across the world in numerous as a secure natural supply of medication. Since the beginning of time, people have relied on plants that could provide for their basic needs things like gasoline, food, shelter, and everyone's health there are several applications for plants, and Therapeutic skills unavoidably contributed to the existence of prehistoric societies, who relied on plants that can treat diseases. The awareness of When first discovered, plants therapeutic properties across generations, orally, and as civilizations.<sup>8</sup> Plants with these characteristics may contribute to the rapid release of fertilized ovaries from the fallopian tube, the suppression of implantation due to a disruption in the oestrogen-progesterone balance, and fatal development. Abortion brought on by inadequate food availability to the uterus and the male through influencing sperm count, motility, and the male embryo, as well as viability. Many employees have reported a lot of in recent years Traditional plants used as contraceptives. Several of the Subsistence farming has been practiced by tribal economies, Piggery, fishing and hunting. Time has passed, and tribes Communities have amassed a wealth of information on use of plants and plant-based remedies to treat a variety of diseases and ailments in this investigation, an effort has been made.<sup>9</sup>

## **[2] MATERIAL AND METHOD**

*P. zeylanica* Linn. Leaves were collected in the Kanyakumari area of Tamil Nadu, and Dr. H. S. Chatree, Botanist, Govt. Arts, positively recognized the leaves & Mandsaur, Madhya Pradesh's Science College. Certificate samples (P/006/2006/BRNCOP) were put in the Department of Agriculture's herbarium future, pharmacognosy, BRNCP, Mandsaur reference.<sup>9</sup>

### Mechanism of action of herbal drugs

Different methods can be used by medicinal plants to cause infertility. They could affect the uterus, the ovary, and the creation of hormones, the inhibition of hormonal action, the implantation process, and the generation of sperm. Some of them create a barrier around an embryo to stop fertilization. These actions allow for the classification of the plants into many groups:

SR. NO	PLANTS	MODE OF ACTION ON REPRODUCTIVE SYSTEM
1.	Antifertility Plants	Prevent fertilization
2.	Antioviulatory Plants	Inhibit ovulation
3.	Anti-implantation Plants	Blocking implantation
4.	Abortifacient Plants	Causing early abortion

- Antifertility medications are those that hinder gamete development and disrupt the process of conception.
- The antifertility medications known as antioviulatory medicines cause infertility by inhibiting the ovulation. These medications are administered intravenously or orally.
- Anti-implantation medications are substances that hinder the adhesion or infiltration of developed egg inside the uterus.
- Abortifacients are drugs that induce the fetus to expel itself early

### [2.1] MARKETED FORMULATION

ALLOPATHIC FORMULATIONS	HERBAL FORMULATION
Vanilic acid	Yogaraja guggulu vati
Trans- cinnamic acid	Chitrakadi vati
Isoshinanolol	Chitraka ghrita
Plumbagic acid	Chitrakadi churna
Indole-3-Carboxaldehyde	Lauhasava

After speaking with locals and practitioners of alternative medicine, plants were gathered between July 2010 and July 2011 throughout each of their many blossoming times. Information on the plants' native names, components used, medication formulation, dosages, and method of use in conventional methods of limiting population expansion were gathered. Plant material was gathered, compressed, and soaked in alcohol for Standard floras were used to identify herbarium vouchers. The information gathered in the field was prepared and saved carefully. Voucher specimens were placed in the herbarium at the Assam University, Silchar, Department of Life Science and Bioinformatics.<sup>10</sup> For the current investigation, a variety of kodiveli samples from the raw medicine markets in Tiruchirappalli and Chennai, South India, were preserved for 3, 6, and 9 months, respectively. Fresh samples were gathered from the gardens of medicinal plants of Tamil Nadu's Puthanampatti and Tiruchirappalli. Brand-new samples were combined with being dried, shaded, and subjected to HPTLC analysis commercial samples. Standard Plumbagin was also HPTLC-tested.<sup>11</sup> According to some workers, treatment with *Plumbago zeylanica* during the first seven days

of pregnancy eliminated the uterine proteins in 13000, 19000, 26000, and 75000 Da molecular weight resulting preimplantation loss in pregnant women. . Proteins with atomic masses of 55,000 and 65,000 Da when rats were administered P after abortion. Powdered zeylanica root from days 6 to 17 of pregnancy. Another study found that the inclusion complex of hydroxyl propyl betacyclodextron and plumbagin (HP $\beta$ CD) was created with the intention of effectiveness and soluble. The complex's antifertility potential was assessed while it was contained inside the aqueous layer of niosomes. Five milligrams per kilogram (mg/kg) intraperitoneally, the complex's niosomes demonstrated positive anti-fertility effects. Niosomes with increased activity in comparison to the control and trapping of the lipid layer. Some researchers found that plumbagin significantly reduced implantation and induced abortion in albino rats without teratogenic effects. Origins of Plumbago According to reports, zeylanica is a potent toxin. When ingested or applied to the ostium uteri, brings about abortion.<sup>12</sup>

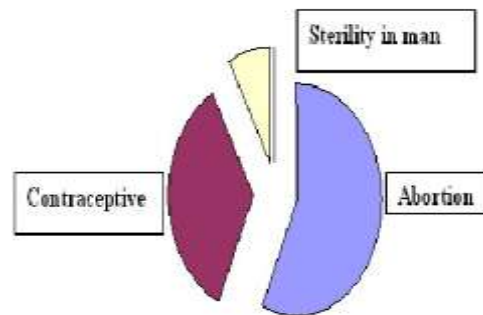
## [2.2] EXTARCT OF LEAVES



**FIGURE 8: SPECIES OF PLUMBAGA**

Due to anti-estrogenic action, a hydro alcoholic extract of *Plumbago zeylanica* leaves demonstrated extremely powerful (95.167%) anti-implantation efficacy. hinders the effects of estrogen, damages structural and uterine functional alterations. Antiestrogenic effects include additionally confirmed by a drop in glycogen content, diameter, endometrial and myometrial thickness, fewer pits and folds along with a smaller uterine lumen the uterine glands' size and quantity had reduced, opening of the vagina and cornification. Edwin et al. and Azad Chowdhury investigated showed *P. zeylanica*'s acetone and ethanol extracts were most efficient way to stop the estrous cycle is to display a

protracted diestrous phase of the estrous cycle causing ovulation to temporarily be inhibited. Added in *P. zeylanica*, a human, serves as a family planner and agents appearing to prevent implantation.<sup>12</sup>



**Figure 8:** Pie-chart showing mode of action of plants

Numerous studies have been conducted to evaluate the pharmacological potential of the plant's various parts, including the roots, stem, flower, and leaves, as antibacterial, hepatoprotective, cancer- and fertility-preventive, ulcer- and wound-healing, antiulcer, and antifungal agents.<sup>14</sup> *Leishmania amazonensis* promastigotes' development was 88% reduced by the ethanolic stem extract at 100 mg/ml. It is bitter, diuretic, expectorant, tonic, and effective appetizer, beneficial for illness, scabies, laryngitis, and rheumatism of the spleen.<sup>15, 16</sup> In order to create a foolproof contraceptive medicine from this significant plant, *Rivea hypocrateriformis* extract must be thoroughly examined for specific phytochemical agents and for specific effects on the target tissue.<sup>17</sup> When *Momordica charantia* seeds were administered orally at a dose level of 25 mg/100g body weight, the pattern of estrous cycle became erratic. Cyclicity and a substantial lengthening of the Reversibility of the estrous cycle in rats.<sup>18</sup> in female Wistar rats, *anethum graveolens* ethanolic extract lengthened the diestrus phases and the entire estrous cycle.<sup>19</sup> when *citrus medica* seeds extracts were administered to albino rats, this resulted in an abnormal estrous cycle with prolonged proestrus and estrous and decreased metestrus.<sup>20</sup> Given to rats at a dose level of 1g/kg body weight, the alcohol extract from *Azadirachta indica* flower caused an irregular oestrous cycle with prolonged period of death. Additionally, lower the frequency of occurrence of the estrus phase with partial ovulation blockage.<sup>21</sup> when albino rats were administered an ethanol extract of *Plumbago zeylanica* leaves, their estrous cycle was interrupted, and they displayed a protracted diestrous stage in line with to a transient ovulation inhibition.<sup>22</sup> When *curcuma longa* was administered to albino rats, it suppressed the oestrous phase and ovulation.<sup>23</sup> Wistar strain female albino rats (150–200 g) with regular estrous cycles and established fertility were housed in cages with males in a 2:1 ratio. The females were looked at. The morning after looking for signs of copulation. The animals, which had spermatozoa in dense clusters in the vaginal smears were divided, and that day was set aside for testing. The first day of pregnancy. The PFAE were suspended were starting on day 1, delivered orally with an intragastric catheter until week 7 of pregnancy, respectively, at 300 and 500 mg/kg bw pregnant rats in various groups. Animals in control received only the car (Tween-80, 1%, p.o.). The creatures were semi-sterile and laparoscopic surgery while under light ether anaesthesia pregnancy day 10 circumstances. Both horns of the uterus were observed for the number and size of implants. The rat was given time to heal and give birth after reaching full term. Every fetus was weighed and checked for obvious flaws. To monitor their postnatal growth, the litters were allowed to grow. And keep an eye out for any congenital abnormalities.<sup>24, 25</sup> Three groups of six rats each were created

from rats that were separated into three groups on the first day of pregnancy. As a control, the first group just received a car (Tween-80, 1%). and *P. zeylanica* PFAE suspension was given to groups 2-3.root (300 and 500 mg/kg, respectively) in 1% Tween-80 from 10 to 18 weeks of pregnancy. Animals were used in the experiment. Were kept an eye out for uterine haemorrhage. Animals on day 21 were laparotomized while sedated with mild ether, and observed for the quantity of litters and the resorption rate in relation to the original number of implantations on the tenth day of pregnancy.<sup>26</sup>

### [3] FORMULATION DETAILS

Shanghai Institute of Planned Parenthood Research (SIPPR), one of the WHO Collaborating Centres for Research in Human Reproduction in China, produced the improved BZK gel. It is a brand-new vaginal gel that is being studied as a form of contraception and a preventative measure against many STIs. 4.2 ml of the BZK gel (0.429%) are placed into a unique disposable container. Each usage of a thruster. A dispersion agent called polydimethylsiloxane is present in the gel, which coats and provides coating and anti-adhesive action to protect the entire vaginal mucosa. It offers dual by serving as a physical and chemical barrier, protection against STIs. The process may take eight hours. Research techniques Pre-clinical research on a variety of drugs, including pharmacological and toxicological tests BZK gel optimization has been done. The three components of these studies were as follows: **I.** Spermicidal activity of BZK gel:

- 1) In vitro spermicidal test;
  - 2) In vivo spermicidal test in rabbits;
  - 3) Anti-fertility test in rabbits;
  - 4) Contraceptive test in rabbits.
- II.** Vaginal mucosal irritation test in rats  
**III.** Microbiological assessments

By using computer-assisted sperm analysis (CASA), the sperm immobilizing activity (SIA) of optimized BZK gel was contrasted with that of 3.5% N-9. High resolution (2.4%, 1.2%, and 0.4%), low voltage imaging was used to assess the impact of BZK gel on sperm membrane integrity. HR-LVSEM, or scanning electron microscopy. In the rat test for vaginal mucosal irritability, the rat vaginal tissue was scored for histologic alterations after 10 consecutive days of BZK gel injected intravaginally.<sup>27</sup> Buffer Gel is a cutting-edge spermicidal and microbicidal gel designed to preserve the vagina's natural protective pH by acidifying semen, which would otherwise alkalinize it. To examine in animal models the effectiveness of Buffer Gel in avoiding pregnancy and STDs. After pre-treatment with the test and control agents, or after no pre-treatment, animals were challenged with pathogens or sperm and then tested for infection or pregnancy using the usual techniques. Buffer Gel demonstrated significant contraceptive efficacy in the rabbit, as well as significant resistance to the transmission of *Chlamydia trachomatis*, cottontail rabbit papillomavirus, and herpes simplex virus type 2 (HSV-2) through the vaginal and rectal routes in mice. *Neisseria gonorrhoea* vaginal transmission was not prevented by it.<sup>28</sup>



### **[3.1] METHOD AND PREPARATION OF VAGINAL GEL**

*Plumbago Zeylanica* Linn. were procured from local market. The roots were shade-dried and then powdered. The powder was then used for extraction using solvents (water: ethanol, 1:1). Hydro alcoholic extract was thus prepared by using a laboratory scale Soxhlet extraction apparatus. Soxhlet extraction was carried out for 48 h. The extract thus obtained was evaporated by heating ( $50^{\circ}\text{C}\pm 2^{\circ}\text{C}$ ) to a constant weight. The vaginal gel, was prepared by soaking a known concentration of the gelling agent in water overnight. The gelling agent was then stirred on an overhead stirrer (Remi Motors) for uniform mixing. The exact quantity of the prepared extract was then added to the gelling agent (1% wt/wt polycarbophil) with stirring to obtain a gel. The final pH of vaginal gel was adjusted to 4.5–5.5 using 10% sodium hydroxide solution.<sup>29</sup> also other method of preparation, For 1% Carbopol 934P (w/v), the necessary amount of Carbopol 934P was dispersed in a small amount of distilled water with vigorous stirring, then 0.1 mL of triethanolamine was added drop by drop until a translucent, clear gel was formed. PH 4.75 phosphate buffer was then gradually added while stirring until fully incorporated to get the desired concentration. The produced gel was continuously stirred as powdered SIF was added until a It was possible to achieve homogenous dispersion (Sangeetha et al., 2012). Many other Using the same process, Carbopol gel at concentrations of 0.5%, 1.5%, and 20% was also created.<sup>30</sup>

#### **[3.1.1] ESTIMATION OF SIF CONTENT AND UNIFORMITY IN VAGINAL GEL**

In 25 ml of simulated vaginal fluid (SVF) made in accordance with Owen & Katz (1999) guidelines, 0.5 g of gel was suspended. The dispersion was filtered and examined at 280 nm with a UV-Visible spectrophotometer. Gel containing all the excipients to counteract any absorbance caused by them. Components excluding The SIF was also the subject of parallel evaluations. The SIF's material was determined by taking samples randomly throughout a single batch of the gel. The gel formulations' consistency in SIF content. Three various batches were examined. The average SIF content/g of the produced gel in the same manner.<sup>32</sup>

#### **[3.1.2] DETERMINATION OF PH**

The electrode was dipped into the gel formulation for 30 minutes after 1 g of the gel formulation had been dissolved in 25 mL of distilled water.<sup>32</sup>

#### **[3.1.3] DETERMINATION OF SPREADABILITY**

Using a custom made assembly based on the design of De Paula et al. (1998), the spreadability of the gel in contrast to KY Jelly was evaluated. Ten equal-sized glass plates (30 x 30 cm), each weighing 200 g, were selected. A 5 g gel mixture was applied. Across a 3.14 cm<sup>2</sup> area in the lower plate's center. In advance weighed glass plates positioned one by one over the gel at intervals of one minute, the spread was measured after each increment. Observed was diameter. The test was run three times, and mean values were computed.<sup>31</sup>

#### **[3.1.4] RHEOLOGICAL STUDIES**

The created SIF loaded hydrogel's rheological behavior was assessed using a cup and bob rheometer (Rheometer HS-143; Rheolab QC, Anton Paar, Germany) Concentric cylinder equipment (Z4 probe with cup and bob radii of 7.59 mm and 7.0 mm) is used for this. Each was filled with around 5 g of

gel (bob cone measurement angle = 120o) Sample. Shear stress was increased linearly from 0.1 to 100 s<sup>-1</sup>.<sup>33</sup>

#### [4] DISCUSSION AND CONCLUSION

This study emphasizes the significance of scientific methods of proper identification and authentication as well as the impact of storage of traditional drugs. These factors can undoubtedly contribute significantly in promoting eco-friendly herbal drugs. The goal of the present study was to develop an analytical method for the estimation of plumbagin, an active chemical constituent of *P. zeylanica*, a traditional drug source. This review's list of medicinal plants like *plumbago zeylanica* that have been utilized as antifertility remedies is helpful for both researchers and clinicians. This is the greatest list utilized only to screen potential candidates in the early stages plants that prevent contraception, not as a comprehensive or final list plants that prevent contraception. Population growth, poverty, and pollution are all related and must all be managed in developing and impoverished nations. Checking human fertility is necessary for population control. The traditional medical system offers us a wide range of ways that stop human reproduction. These hormonal contraceptives include condoms, intrauterine devices, birth control pills, skin patches, and more. They are difficult for developing countries to access since they are pricey, inaccessible, and containing chemicals that could have negative effects on the person's body. Consumption of medications made chemically must be prevented and minimized. Then, folks ought to favour natural medications. The majority of therapeutic herbs and other plant extracts are included. Herbal extracts can affect fertility in a variety of ways, including may interfere with or negatively impact female reproductive organs such the ovaries, uterus, etc. due to the fact that they include phytoestrogen, progesterone, or analogues therefore, as well as other plant extracts.

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