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A Comprehensive Review on the Anti-Fertility Potential of Plumbago Indica

Gayatri Khosla[1], Disha Dutta[2], Swati Srivastava[1], Swati Madan[3], Shikha Saxena[3], Rama Tyagi[1*]

[1]Galgotias College of Pharmacy, Greater Noida, U.P., 201310, India
[2]IIMT College of Pharmacy, Knowledge Park III, Greater Noida
[3]Amity Institute of Pharmacy, Amity University, Noida, Uttar Pradesh 201303, India

ABSTRACT: Creating a comprehensive list of medicinal herbs that are used by different nations and folklore groups all over the world as anti-fertility agents in females was the overall objective of this study.By researching through classic textbooks and peer-reviewed articles, as well as accessing well-known international scientific databases, we conducted a full bibliographic investigation. Plant activities such as "antifertility," "anti-implantation," "antiovulation," and "antispermatogenic" were searched for in CENTRAL, The Embase database, and PubMed. The search phrases that were used were "antifertility," "anti-implantation," "antiovulation," and "antispermatogenic."Antifertility agents are plants, as well as their components and extracts, that have traditionally been used to aid in the treatment of infertility. The analysis of Plumbago indica for further study in this article suggests that many of these medicinal plants have antizygotic properties. This research primarily demonstrates that further investigation into plant extracts and active chemicals is necessary to better understand their mechanisms. It is now time to expand experimental studies to identify new, likely chemical components from medicinal plants. Through this effort, an adequate basis has been established for further research on the efficacy of plants that women presently use as conventional antifertility therapies but that, with greater research and analysis, have the potential to become effective antifertility drugs.

1. INTRODUCTION

Medical products that control fertility include oral contraceptives, which are also referred to as antifertility drugs. These medications can change and influence both the ovulation and menstrual cycles of females.
In birth control pills, oestrogen and progesterone are combined in equivalent amounts [1]. It is deemed active when an antifertility drug prevents fertilisation, ovulation, or implantation, kills the embryo, or causes abortion in females. It affects male sperm lethality or organ gonadotrophin, slows sperm formation, and decreases testosterone. The size of the population is now controlled in many emerging nations [2]. Oxyphenbutazone, indomethacin, and acetyl salicylic acid are all substances that have been shown to reduce the formation of prostaglandins and have antifertility effects against albino male and female rabbits. Indomethacin and oxyphenbutazone, as well as male rabbits, appear to affect the reproductive process. Antiovulatory effects were observed in rabbits exposed to acetyl salicylic acid at a dosage of 300 mg/kg and indomethacin at a dosage of 3 mg/kg. Indomethacin also has anti-implantation effects. This demonstrates that nonsteroidal anti-inflammatory medications have an impact on female animals' reproductive systems. Antimalarial drugs have been reported to have anti-fertility characteristics because amodiaquine suppresses ovulation and breaks the oestrous cycle [3]. Medicinal herbs are a great gift from nature that may be utilized to heal a variety of human problems. In the rapidly growing sector of science and technology, some South Asian universities have long been developing the talents of future generations [4].

In that province, a lot of scientists are working to create the next generation of scientists in order to support the field's future growth. They are also collaborating with venture capitalists and the business community in order to maximize their research potential. Herbal treatments and their derivatives have been utilized in traditional medicine nearly from the beginning of time [5-10]. Modern scientific study has decisively proved the curative potential of Therapeutic plants. However, the wider use of

therapeutic plants has only recently begun to acquire acceptance in the greater international arena. Various hurdles must be solved before they may attain their full commercial potential, such as absence of quality assurance as well as research related to toxicity, with the requirement to extend product shelf life, and compliance with international regulatory requirements, to name a few. A variety of medicinal plants contain anti-fertility properties (Table 1). Unani medicine, which is a part of South Asian culture, is practiced by a substantial number of the populations of India, Pakistan, Bangladesh, and Sri Lanka. [11, 12]. As a result of its regional appeal, unani medicine has expanded tremendously in popularity throughout South Asia over the last five decades. The creative nature of Unani medicine lies in the fact that its clinicians have accepted and surmounted many of the difficulties faced by practicing physicians, including issues with practice-patient relationships, intervention techniques, and the conceptualisation of sickness. Though still in use among tribal cultures, the knowledge that is now used to regulate conception requires more scientific investigation so that the active components found in such plants that are capable of impeding the reproductive cycle can be effectively identified and exploited. Over 65% of Pakistan's population uses unani medicine, which has stayed common in a number of South Asian nations [13-17]. The global pharmaceutical market is expected to earn nearly $ 115 billion in 2015, according to the Worldwide Industry Analyst Market, driven by the trend toward herbal and natural resources, which is based on the premise that these products have fewer adverse effects than contemporary medicines. Around 75% of the population in emerging countries receives herbal medical health care, compared to more than half of the population in affluent countries, particularly for lifestyle-related diseases [18]. As a result of a structural change in how the herbal medicine industry might offer financial advantage for different nations and corporate sectors [19], more firms are providing medical coverage for herbal medical care. The lack of educational institutions for herbal medicine and the comparatively low level of funding allocated to study and progression are two significant obstacles to company growth. Regarded as a kind of herbal medicine institution education, several healthcare providers in the conventional medical field are ignorant of the degree of danger connected with alternative therapies. Medicinal herbs' anti-fertility properties, as well as their usability in experimenting human ailments regarding which they garnered a worldwide credibility, have been empirically proven over a long period of time all over the world. The anti-fertility effects of medicinal herbs have been studied; for example, several components of different plants contain oestrogen and have varying effects on different life processes [20]. Estrogen-like substances found in a variety of plants are known as phytoestrogens. They are poisonous to domestic animals and disturb the typical pregnancy process, resulting in sterility. The world population is inevitably expanding day by day due to a widespread shortage of family planning and help [21]. There are a range of family planning options available, but each has its own set of disadvantages. Some anti-fertility drugs stop spermatogenesis altogether, resulting in irreversible infertility. Vaccines can also regulate the amount of fertility in both males and females. The active mechanism in such a vaccination is the formation of antibodies against human chorionic gonadotropin, although it causes sterility in male animals [22]. Furthermore, anti-fertility drugs slow down the spermatogenesis process in males. Currently used anti-fertility medications include triptolide, tamoxifen, gossypol, and testosterone [23]. Clinical researchers studying ethnopharmacology are becoming more and more common in developed nations like Europe and North America. Some of the medicinal plants described show promise and could lead to the development of drugs that are as effective as the current medicine [24]. Furthermore, considering its negative effects, misprostol is an inexpensive and efficient abortifacient that may be administered sublingually or orally in an allopathic approach. Many people are apprehensive to utilise allopathic medications because of their known side effects. There may be benefits to utilising a range of plants/preparations to manage fertility, according to an assessment of the studies. There is also evidence of some locally available contraceptives in conventional medicine. Studies on medical plants that are frequently used as antifertility treatments or have been investigated for their effectiveness in vitro in addition to in vivo have been conducted. Plumbago indica belongs to the Plumbaginaceae family, which includes 10-20 Plumbago flowering plant species. Wild plants known as Plumbago indica (White Leadwort) can be found in Sri Lanka and India. (Especially in Bengal, Uttar Pradesh, and South Indian provinces). Around the globe, it can be found in both temperate and tropical climates. Plumbago indica is likely to have originated in Southeast Asia [26, 27]. When fully grown, an evergreen plant can grow to a height of 6 feet, but with proper pruning and the right receptacle, the size of the plant can be controlled. With temperatures ranging from mild to warm, the plant loves full sun to moderate shade. For hundreds of years, rural and tribal cultures have used it as traditional medicine [28]. The name "plumbago indica" alludes to the tendency of plant sap to leave lead-colored spots on skin and comes from the Latin words plumbum (lead) and agere (to resemble) [29]. Plumbago indica has a long and illustrious history reaching back to the Vedic era. The term Chitraka (Hindi) was used by Charaka (1500 B.C.) to describe a chemical that induces skin colouring when applied topically [30].

The chemical makeup and application of therapeutic plants are the focus of research by all science disciplines. This research may lead to the development of more avant-garde products with fewer side effects than presently available medications [31]. Researchers are also intrigued by the huge variety of natural product designs as well as their physicochemical and biological characteristics. However, the possibility of only few plants as medications has been studied unless they are used for local medical requirements. The evidence is therefore insufficient to indicate any real promise [32-35].

Numerous research groups have investigated the biological functions of medicinal plants from around the globe. These studies are founded on how various species have been used traditionally [36], along with raising public awareness, scientific research has been done on the use of medicinal plants, with an emphasis on how these plants might benefit the pharmaceutical business. Natural ingredients were present in about half of the drugs that were authorized between 1981 and 2006 [37].

Extracts' chemical intricacy is essential for the formulation's effectiveness because it must also allow the active ingredient to be released. Therefore, carriers must control active absorption and biological reaction while also boosting the drug's solubility, cutting down on degradation and toxicity, and masking any unpleasant flavors. [38-39].

Numerous medicinal plant products' chemical make-up and biological properties have previously been determined through phytochemical and phytopharmacological study. The majority of biologically active components in extracts, like flavonoids, tannins, as well as terpenoids, have higher amount of solubility in water but rather have lower absorption because of their poor absorption, failure to cross lipid membranes, and large molecular sizes. A decrease in bioavailability and effectiveness is the outcome. In vitro experiments have demonstrated the effectiveness of herbal medicines, but in vivo research has not yet supported these findings. Many crucial substances are also infrequently used in formulations due to their undesirable qualities or compatibility issues with other compounds [40-41].

Numerous nanotechnological methods, such as nanoparticles of solid nanoparticles of lipids (SLNs), liquid crystal (LC) networks, precursors regarding liquid crystals (PSLCs), liposomes are as well as microemulsions, are all being developed in an attempt to get beyond this obstacle. These methods make it possible to combine materials with different qualities into a single formulation and can even change a material's characteristics and activity in a biological setting. These technical advancements have had a significant impact on how medications are delivered.

The efficacy of active compounds may be enhanced by the new drug transport techniques, and components that were previously dropped from formulations due to their inutility may also be added back. This strategy also works because of the capacity to develop new goods before they are marketed or utilised therapeutically, such as boosting selectivity and efficiency, minimising heat or image degradation, lowering side effects, and managing the release of active substances [42-46] Scientific advances in nanotechnology as well as nanoscience are desperately needed in relation to the use of nanoscale materials, and this have historically been the sole domain of the cosmetics industry. Science has made it possible to create innovative solutions to challenging issues in the mixing process. Nanostructures can effectively combine active compounds with various levels of hydrophilicity and lipophilicity, as well as increase the solubility and stability of active ingredients. Using this method, a substance's distribution to specific tissues or systems can be controlled [47-49].

Nanotechnological advancements are appealing to the pharmaceutical industry because they enable advantages like new release methods and the creation of formulas that weren't previously possible.

Although nanotechnology has benefited several medical fields, some drawbacks need to be addressed. Clinical researchers have identified a number of drawbacks, including high costs, challenges scaling up procedures, and nanoparticles' easy infallibility, which can cause severe lung illnesses and frequently result in other diseases that change homeostasis or result in death [50].

Scientific Classification

Kingdom: Plantae

Phylum: Tracheophyta

Class: Magnoliopsida

Subclass: Caryophyllidae

Superorder: Plumbaginanae

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Order: Plumbaginales

Family: Plumbaginaceae

Genus: Plumbago

Species: indica

Common names

Chitraka (Hindi-UP), Telhidakangouba (Manipur), Chittiramoolamkarimai (Tamilnadu).

DESCRIPTION OF THE PLANT

Plumbago indica is a minuscule, 3-4-foot-tall perennial plant that is evergreen. The leaves are 4-10 cm long, pointy at the tip, and oblong, hairy-edged, dense, flamboyant, intuitive, alternating, and spirally orientated. From September to November, flowers blossom. The white blooms are between 10 and 25 cm tall [51]. The inflorescence is an enduring raceme, and the bracts are oval to lanceolate, ovate to lanceolate, ovate to lanceolate, ovate to lanceolate, ovate to lanceolate, ovate to lanceolate, ovate to lanceolate, ovate to lanceolate, ovate to lanceolate, ovate to The fruits are rather similar. Fruit is a 5-furrowed, 1-seeded rectangular capsule with a sharp apex. The seed is oblong, measuring 5-6 mm in length and ranging in visual appearance from reddish brown to dark brown. The roots are robust, cylindrical, friable, and blackish red, bearing a pungent smell.

Pharmacological characteristics

In India and Asia, plumbago indica is widely used to treat condition regarding skin, illnesses, and intestinal worms. Inflammation, leprosy, scabies, ringworm, dermatitis, ulcers, hemorrhoids, and hookworm are among the clinical conditions connected to the plant [54]. Although the entire plant is used, the roots' special therapeutic characteristics have captured the attention of scientists and biologists. The plant was used to cure gonorrhoea, syphilis, TB, arthritis pain, swellings, and healing despite the fact that the pulped roots and aerial parts were thought to be abortifacient [55]. To ease inflammation in the mouth, throat, and chest, drink a root infusion with boiling milk. An infusion of the root is used to cure shortness of breath, while a paste of the root mixed with vinegar, milk, and water is used to treat influenza and black water fever [56]. The plant has been demonstrated to have strong anticancer, [57] antitumor, [58] antiinflammatory, [59] antioxidant, [60] antimycobacterial, [61] and antibacterial effects in the Ayurvedic and Unani medical systems. Rheumatic pain, sprains, scabies, skin problems, and wounds are all treated with this herb. The plant's roots and components have antiatherogenic, cardiotonic, and hepatoprotective properties. Plant extracts have been demonstrated to have strong mosquito larvicidal activity against Aedes aegypti larvae. Hexane extracts of Plumbago indica show anti-canine distemper virus activity. **Plumbago indica** acetone extract has been shown to reduce chromosomal abnormalities caused by ethinylestradiol in cultured human cells. The root is used to manufacture "yogarajguggal," an herbal combination that is used to treat arthritis, rheumatism, and other diseases. Stimulant, caustic, digestive aids, antiseptic, antiparasitic, and parasite killers are all utilised in medicine with roots, root barks, and seeds. Plumbagin, a major component found in the roots and leaves of Plumbago indica, has been identified as a significant bioactive component linked to a variety of pharmacological activities, including antitumor, [30-32] antimicrobial, anticancer, wound healing, [33] anti-inflammatory and altered T-cell proliferative activities, [34, 35] and antifertility actions [36-40]. It's also a powerful irritant. It possesses sudorific qualities and, in small doses, activates the central nervous system.

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Figure 1: Various mechanisms of antifertility agents

PLUMBAGIN'S PHARMACOLOGICAL PROPERTIES

Plumbagin

Antibacterial activity [42], antitumour activity [31], antifertility activity (Figure 1) [39], antitumor and antifertility activities [32], synergistic activity [18], anticoagulant activity [59], hypolipidaemic and antiatherosclerotic [56], GST activity [16], oxidative stress [86], synergistic activity [18], anticoagulant activity [59], hypolipidaemic and antiatherosclerotic [56], GST activity [20] Antibacterial activity Activation of blood coagulation [61] Activity against Helicobacter pylori [41]

Phytochemistry

Using thin-layer chromatography, alkaloids, phenols, and flavonoids were found in crude extracts of PZ. PZ produces lineleic acid, palmitic acid, nonylnonanoate, stigmasterol acetate, lupeol acetate, friedelinol, lupeol, lupanone, sitosterone, and stigmasterol, according to phytochemical screening [42]. High concentrations of four elements (Na, K, Ca, and Mg), key microelements (Zn, Fe, Mn, Cr, and Co), and eight additional elements (Mo, Sb, Bi, Cd, Sr, Pb, Cd, and as) were found in PZ leaves, stems, and roots, all of which were identified using inductively coupled plasma atomic emission spectrometry (ICP-AES). These chemicals are commonly found in anticancer and antioxidant therapy. Using column chromatography, plubagin and indole-3-carboxaldehyde were extracted from the aerial portions. 88 Beta-sitosterol, beta-sitosteryl-3betaglucopyranoside, beta-sitosteryl-3betaglucopyranoside- 6'-O-palmitate, lupenone, lupeol acetate, plumbagin, and trilinolein are all found in the dichloromethane extract of aerial parts. Plumbagin, the active component, was isolated from several PZ plant parts by RP-HPLC89, as was the production of the binaphthoquinone 3, 3'-biplumbagin. Reverse phase HPLC with UV detection, liquid chromatography, and tandem mass spectrometry were used to determine plubagin quantities. Antifertility herbs are herbs that are used to treat infertility.

Anti-Ovulation Behaviour

Formic acid, acetic acid, beldianic acid, tannin, essential oil, and oxymethylanthraquinones are among the active compounds found in the roots and leaves of the esteemed Polygonaceae plant known as Plumbago indica Linn. Haemorrhoids, dyspepsia, skin conditions, and diarrhoea are treated with it. These compounds have antibacterial, anti-inflammatory, anti-fertility, and antioxidative actions in humans. In one study, Kapoor et al looked at the anti-ovulatory properties of this herb (Figure 2). They

employed three types of extracts to investigate the herb's anti-fertility effects (petroleum, aqueous, and alcohol). Rabbits with copper-induced ovulation showed anti-fertility action.

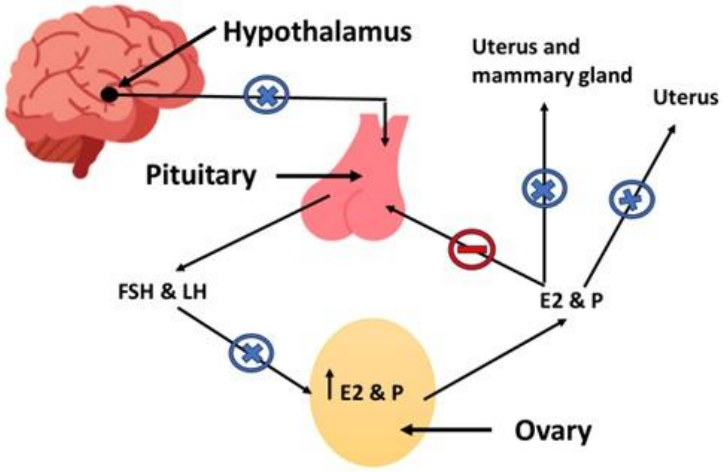


Figure 2: Mechanism of action of antifertility drug

Table 1: Pharmacological activities of some solvent extracts of Plumbago indica herb.

Table 2: Plumbagin has been investigated in vivo and in vitro for anticancer and antiproliferative properties.

Plant extract type	Dose	Negative Control	Animal model / Microorganisms	Duration	Results	References
Leaf extract in MeOH	25, 50 & 100 Mg	-	Indian earthworm (Pheretimaposthuma)	2 days	Anthelmintic activity	33
Leaf extract in MeOH	50,100, &150 µg/ml	-	Helicobacter pylori	1 day	Anti- bacterial activity	34
Ethanol, acetone or ethyl acetate of Rhizome	30 µl	-	Helicobacter pylori	3 day	Antibacterial activity	13
Root extract in MeOH	0.64-10.24 mg/ml	Ethanol	E. coli and Shigella	2 days	Anti- bacterial Activity	35
Plumbago indica root	100 mg/kg	-	Human study	14 days	Anti- hyper Cholesterolemic activity	34

Stem extract in MeOH	500, 1000 mg/kg	48/80	Wistar Mice	2 days	Antiallergic activity	21
			Staphylococcus aureus, Bacillus subtilis, Escherichia coli, Pseudomonas			
MeOH, chloroform and alcoholic extracts of leaves	50, 100 mg/ ml		aeruginosa		Antibacterial activity	
		-		1 day		41
MeOH, Chloroform and	1 mg/ml	-	E. coli, Salmonella typhi, Klebsiella	2 days	Antibacterial activity	23
aqueous extract of root			pneumoniae, Serratia marcescens, Proteus vulgaris, Pseudomonas aeruginosa, Staphylococcus aureus, Bacillus cereus			
Petrol. ether, ethanol and aqueous extract of root	1200 µg/ml	-	S aureus andM. luteus	2 days	Antibacterial activity	39
			B. subtilis, S. aureus, E.			
Leaves extract in MeOH	50, 100 mg/ml	-	coli and S. typhi	2 days	Antibacterial activity	33
Root extract in Methanol	100, 200 mg/kg	Cancer cell line	Swiss albino mice	14 days	Anticancer activity	36

Root extract in ethanol	250 mg/kg bw	3-methyl-4- di methyl amino azo-benzine	Wistar albino rats	7 days	Anticarcinogenic activity	37
Hydroalcoholic extract of leaves	250, 500 mg/kg	PTZ	Wistar albino rats	1 hour	Anti-convulsion activity	38
Root extract in MeOH	4-10 mg/ml	Occluded dermal irritation	Albino rabbits, Swiss mice	1 day	Anti-dermatotoxicity	60
Root extract in ethanol	250 mg/kg bw	Alloxan	Wistar albino rats	21 day	Antidiabetic activity	18
Root aqueous extract	100, 200 mg/kg	STZ	Wistar albino rats	42 day	Antidiabetic activity	39
Aqueous extract of Leaves	100, 200 mg/kg	STZ	Wistar albino rats	28 day	Antidiabetic activity	40
Leaves aqueous extract	100, 200 mg/kg	STZ	Wistar albino rats	28 day	Antidiabetic activity	41
MeOH, chloroform extract of whole plant			Rhizoctonia solani Kuhn, Bipolarisspp., Ustilago maydis and			
			Alternaria alternate	2 day	Antifungal activity	42
	50 µl	-				
Root extract in ethanol	250, 500 mg /kg bw	CYP	Swiss albino mice	7 day	Antigenotoxic activity	54
Petroleum ether extract of root	300 mg/kg	Paracetamol	Wistar albino rats	7 days	Antihepatotoxic activity	43
MeOH extract of aerial parts	35, 70 mg/kg	CCl4	Wistar albino rats	14 days	Antihepatotoxic activity	36

Root aqueous extract	20,40, and 80 mg/kg	Diet-induced hyperlipidemic rats	Wistar albino rats	7 days	Antihyperlipidemic effect	17
Root extract in MeOH	300, 500 mg /kg	Carrageenan	Wistar albino rats	7 days	Anti-inflam-matory activity	46
Pt. ether, chloroform and acetone extract of			S. typhi, S. aureus,			
Root	0.1 ml	-	E.coli,	2 days	Antimicrobial activity	44
			A.niger, Pencilliumsp. And Fusariumoxysporum			
Root extract in MeOH	7.5 mg/ml	RPMI & Dimethyl Sulfoxide	Sprague- Dawley rats	3 hours	Antimutagenic effect	45
Root powder	7.5 mg/kg bw	Phenyl-hydrazine	Wistar Albino rats	21 hours	Antioxidant activity	46
		DPPH(1,1-di				
		phenyl -2-picrylhydrazyl)ABTS (2,2-				
		azinobis-3-ethy lbenzothiazo line-6-sulfonic acid diammoni				
Ethanolic extract of root	1 mg/L	um salt	In-vitro study	1 hour	Antioxidant activity	26
Ethanolic extract of Root	100 mg/kg	-	In-vitro	2 hours	Antioxidant activity	47
Leaves extract in MeOH	50,100 mg /ml	Butylated hydroxy anisole	In-vitro	2 hours	Antioxidant actvity	33

			coxsackievirus B3 Nancy (CVB3), influenza A virus Hong Kong/1/68 (H3N2), and herpes simplex virus type 1Kupka (HSV-1)			
Root extract in MeOH		Guanidine hydrochloride, amantadine, and phosphonoformic acid				
	0.8-200 µg					
	/ml			2 days	Antiviral activity	48
Ethanolic extract of Root	250 mg/kg	Cholesterol	Rabbit	28 days	Hypolipidaemic Activity	50
Ethanolic extract of root		Diet-induced hyperlipidemic			Hypolipidemic activity	
	250 mg/kg	rats	Rabbit	28 days		51
Ethanolic extract of Root	250 mg/kg bw	-	BALB/C mice	6 weeks	Immunomodu-latory activity	52
Aqueous root extract	4 mg/ml	Turkey egg albumin	Balb/c mice	56 days	Immunosuppr-essive activity	53
Chloroform extract of root	100, 200 & 400 mg/kg.	Scopolamine	Swiss albino mice	10 days	Memory Enha-ncing effect	54

Cancer Cells	**Results**	**References**
Human Prostate cancer cell (PC-3, LNCaP, and C4-2)	Reactive oxygen species (ROS) are produced, apoptosis is triggered, and intracellular GSH is depleted.	55
	Reduced cyclin B1, cyclin A, Cdc2, and Cdc25C levels while raising inactivated phosphorylated Cdc2 and Cdc25C levels, increased activation of apoptotic signal-regulating kinase 1, JNK, and extracellular signal-regulated kinase 1/2 (ERK1/2), and finally inhibited ERK and JNK.	
Human Melanoma A375.S2		56

Human non-small cell lung cancer cells, A549	JNK activation and the JNK selective inhibitor SP600125 (Anthra [1,9-cd]pyrazol-6(2H)-one- 1,9-pyrazoloanthrone) reduced apoptosis by preventing p53 phosphorylation and, as a result, enhanced p53-MDM2 interaction. Bcl-2 (Ser70) phosphorylation was likewise inhibited by SP6000125.	
		57
Human Peripheral blood lymphocytes	Has cytotoxic effects, inhibits cell development, induces apoptosis, produces single-strand DNA breaks, and inhibits cell division	58
	Inhibition of (a) protein kinase Cepsilon (PKCepsilon), phosphatidylinositol 3-kinase, phosphorylated AKT, phosphorylated Janus-activated kinase-2, and phosphorylated signal transducer and activator of transcription 3 (Stat3) expression; (b) DNA-binding activity of transcription factors activator protein-1, nuclear factor kappa B	
Human Prostate Cancer		
		59
Human acute promyelocytic leukemia cells	Inhibition of NB4 cell proliferation, chromosomal condensation, and apoptotic body generation in APL cell line NB4 cells, cell proliferation, and induction of apoptosis	
		60
MCF7 and Bowes cancer cell lines	Both MCF7 and Bowes cell proliferation are slowed.	53
Human hepatoma	Certain glycolytic enzymes, as well as gluconeogenesis, are blocked.	37
Human peripheral blood mononuclear cells	Involve the regulation of cell cycle progression, interleukin-2 and interferon production	61
MDA-MB-231 cells	Protein levels of p-PI3K, p-Akt, p-JNK, p-ERK1/2, MMP-2, MMP-9, VEGF, and HIF-1 are all suppressed	54
Human breast cancer cells	Inactivation of NF-kappaB and Bcl-2	53
Human breast cancer cells	Inhibit Akt activity and enhanced the activation of Chk2, resulting in increased inactive phosphorylation of Cdc25C and Cdc2.	54
	In A549 cells, it boosts p53 expression and phosphorylated p53 (Ser15 and Ser392), regulates cell cycle-related enzymes, and activates JNK.	
Lung A549 cells		57
Human ovarian cancer cells	Binds to the active site of ER and inhibits traditional ER signalling pathways.	55

	In C33A cells, a lower dose of radiation coupled with plumbagin may be more effective at inducing apoptosis and caspase 3 activation. Apoptosis is triggered by irradiation and involves caspase-dependent processes.		
Cervical cancer cells		56	
	Increased ROS causes apoptotic cell death and reduces tumour growth without inflicting damage, as well as stimulating mitochondria-dependent apoptosis in tumour cells.		
Human promyelocytic leukemia cells		51	
Ovarian cancer cells	The loss of mitochondrial membrane potential causes nuclear condensation, DNA fragmentation, and morphological changes	57	
	The loss of mitochondrial membrane potential as well as morphological changes associated with apoptosis, such as phosphatidyl serine translocation, nuclear condensation, and DNA breakage, were caused by the generation of reactive oxygen species (ROS) and subsequent induction of apoptosis.		
Human cervical cancer			
		58	
Sarcoma-180	The Ehrlich ascites model was examined and determined to be less dangerous, as evidenced by LD50 survival trials and research.	59	
Azoxymethane induced intestinal	Promising chemopreventive agents for human intestinal neoplasia	50	
carcinogenesis			
	Activated PI3-kinase and/or PDK1 stimulate Akt activity with Ras- Raf-MEK1/2-ERK1/2 pathway		
3T3-L1 cells		41	

CONCLUSION

This study aims to promote the usage of extracts and plants with anti-fertility characteristics. The effectiveness of anti-fertility drugs made from therapeutic herbs has already been shown. There have been numerous plant activity mechanisms found. More investigation is required to better comprehend the bioactivity of other compounds present in crude extracts and to utilize their potential as anti-fertility medications. Therefore, by carefully analyzing the bioactivity of various chemicals, novel and potent drugs can be developed. To increase the effectiveness of recently discovered treatments, increase their selectivity and bioavailability, or decrease their toxicity, drug discovery and delivery are currently being done in tandem. Delivery techniques not only increase the effectiveness of active substances but also enable the re-examination of several substances that have previously been disregarded owing to ineffectiveness. This is a brand-new method with a bright future. Additionally, it helps pharmaceutical firms to assess potential drugs that had previously been ruled out. This is particularly true in the antibiotic industry, where problems with solubility have made it difficult to employ once successful drugs. This subject may be revitalized by better drug delivery system targeting, particularly for species that are multidrug resistant.

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