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Highlights

Impact of Medicinal Plants Antifertility Activities A Review

Discovering Thoughts, Inventing Future

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Impact of Medicinal Plants on Antifertility Activities: A Review

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Abstract- *Aims and Objectives:* The effectiveness of medicinal plants in treating a wide range of illnesses is well known, frequently outperforming that of allopathic medicine. The purpose of this review is to clarify these plants' and their chemical components' anti-fertility characteristics. It gathers current research on medicinal plants with anti-fertility properties that have been verified by science.

Methodology: An extensive bibliographic analysis was conducted, encompassing classical textbooks, peer-reviewed articles, and reputable global scientific databases. Searches were performed in Central, Embase, Niscair, Scopus, Google Scholar, and PubMed using keywords related to the antifertility activity of plants.

Results: Medicinal plant species from various families that have historically been used as antifertility agents in both males and females are included in the review. It describes the different plant partsleaves, fruits, roots, bark, and stems that are used to control fertility.

Keywords: *antifertility, medicinal plant, reproductive systems, antifertility agents.*

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Impact of Medicinal Plants on Antifertility Activities: A Review

Venkataramanaiah Poli [α] & Srinivasulu Reddy Motireddy [σ]

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Results: Medicinal plant species from various families that have historically been used as antifertility agents in both males and females are included in the review. It describes the different plant partsleaves, fruits, roots, bark, and stems that are used to control fertility. The study also offers details on the chemical components, parts used, solvents used, botanical names, and families of these therapeutic plants.

Conclusion: In conclusion, it is evident that medicinal plants serve a significant role as antifertility agents, prompting further investigation into the specific plants responsible for these effects.

Keywords: antifertility, medicinal plant, reproductive systems, antifertility agents.

I. Introduction

One of the most important modern phenomena that demands careful thought is the astounding rise in the world's population. Between 6 and 7 billion people are thought to live on the planet today. The exponential growth of their populations is a significant problem for developing countries like India. An imbalance in socioeconomic infrastructure is likely to result from this population boom's negative effects on social and economic policies. Since human fertility is limited, controlling it becomes a vital and pressing biosocial and medical concern. Many medications, including hormonal and other compounds, have been developed in response to the need for fertility control. To mitigate the potential adverse effects associated with chemically synthesized drugs, there is a preference for indigenous plants, which are not only cost-effective and readily available but also considered safe (1).

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Often known as oral contraceptives, antifertility agents are medications that control fertility (2). These drugs affect women's ovulation and menstrual cycles. Estrogen and progesterone are commonly found in birth control pills. The active ingredients in these antifertility medications work on females by blocking ovulation and implantation, preventing fertilization, and either killing the zygote or causing abortion. These substances function in males by influencing gonadotropins and sperm viability, lowering testosterone levels, or suppressing spermatogenesis (3). Population growth presents serious problems for natural, social, and economic resources (4). The pressing need for efficient contraceptive methods is highlighted by the growing population in developing countries (5).

It has long been known that medicinal plants are useful tools for treating a variety of human health conditions. These plants have been used for centuries to treat physical and mental illnesses; in developing nations, about 80% of medical treatments are used. 6. This field is aided by phytoestrogens, which are novel compounds present in a variety of plants. Furthermore, a number of medications, such as testosterone, gossypol, tamoxifen, and triptolide, are being investigated as antifertility agents (7). Oral contraceptives, also referred to as antifertility agents, are medications that control fertility (2). These drugs affect women's ovulation and menstrual cycles. Estrogen and progesterone are commonly found in birth control pills. The active ingredients in these antifertility medications work on females by blocking ovulation and implantation, preventing fertilization, and either killing the zygote or causing abortion. These substances affect gonadotropins and sperm viability, lower testosterone levels, or inhibit spermatogenesis in males. Many developing nations are currently controlling their populations (3). By interfering with a number of normal reproductive processes in both males and females, antifertility medications reduce fertility. 100% effectiveness, reversibility of effects, lack of side effects, and ease of use are the best qualities in a contraceptive agent (8). Due to a lack of written records, a lack of scientific validation, and comparatively low economic resources within these traditions, these traditional knowledge systems have started to deteriorate over time.

It has been determined that a wide variety of plant species can influence fertility (9). Traditional

medicine has long used plant-based remedies to manage fertility in many places, such as Ethiopia and India. Numerous medicinal plants have been used to treat a range of conditions, including infertility, in addition to being used as dietary supplements, frequently without a thorough understanding of their mechanisms (10). A considerable number of herbal plants also show varied degrees of toxicity, even though many of them have a variety of antifertility qualities, including oestrogenic, spermicidal, ecbolic, abortifacient, and anti-implantation effects (10). Numerous products made from plants have the ability to reduce fertility in both men and women, which raises the possibility that they could be developed as forms of birth control. Only a small number of native plants have had their antifertility effects thoroughly studied, despite evidence that many of them can prevent conception. To find new oral active non-steroidal contraceptive agents, the World Health Organization (WHO) formed a task force on plant research. Numerous medicinal plant extracts have been tested for their ability to prevent infertility in both sexes (11).

It is not a new idea to create safe and efficient oral fertility-regulating substances for human use that are derived from higher plants. Almost all indigenous cultures have used a variety of plants to try to manage population growth for centuries. Many plants have the ability to regulate fertility. There are currently initiatives underway to turn these plants into antifertility products. Economically disadvantaged populations could greatly benefit from plant-based contraceptive methods, such as crude extracts or scientifically validated composite preparations, as these options would be more affordable. The possible abortifacient and antifertility effects of many plants, including those traditionally used in folk contraceptives, are the subject of extensive research worldwide (12).In light of the negative consequences of traditional approaches, fertility control, including contraception and infertility treatment, is an important component of reproductive health for both men and women (13). Numerous efficient techniques for causing infertility have been investigated over time, such as hormonal, chemical, and immunological approaches (14). However, women are less likely to accept chemical methods because they frequently result in a number of side effects, including obesity, gallstones, gastrointestinal problems, and an increased risk of breast and cervical cancers, asthma, and thromboembolism. Hormonal contraceptives are also linked to an increased risk of cancer. Because of their negligible or nonexistent adverse effects, scientists are therefore becoming more interested in plant-derived products as a major source of naturally occurring fertility-regulating agents (15). Health, population growth, and women's empowerment are all directly correlated with the rising use of contraceptive methods (16). In both males and females, a variety of herbal plants have antifertility effects (17).

In recent years, population control has become more and more important. There are many different synthetic contraceptive methods available, but the side effects that come with them frequently limit their long-term use. Both male and female populations have been the focus of efforts to prevent conception. The goal of research in the field of male contraception is to find spermicidal agents that work. On the other hand, female contraception consists of several steps that can be controlled with medication, such as ovulation, fertilization, implantation of the fertilized ovum, and the final maturation of the fetus. As a result, methods to interfere with fertilization have mostly focused on these phases using different substances that are said to be abortifacient, antiovulatory, or anti-implantation. Although there are currently alternatives like steroidal pills, injections, IUDs, barrier methods, and sterilization techniques, the changing lifestyle and growing population challenge suggest that the perfect contraceptive solution has not yet been found (18). The exponential growth of the human population, which can negatively impact economic policies and destabilize financial structures, is one of the major issues facing developing countries. Thus, it is crucial to keep an eye on population growth (19). The demand for herbal remedies made from medicinal plants has increased due to the high cost of new medications, their inaccessibility in remote areas, and the many negative effects of current synthetic fertility control methods, including weight gain, hypertension, hormonal imbalances, and an increased risk of cancer. According to research, women use contraceptives at a higher rate than men worldwide, especially in rural and developing areas where access to contemporary contraceptives is restricted. For women, especially those living in rural areas of developing nations with high population densities like Bangladesh, China, India, and Africa, herbal contraceptives provide an affordable and easily accessible alternative. These substitutes are distinguished by their lower adverse effects and possible efficacy. However, because herbal medicines may pose minor risks, extensive testing is necessary to determine their safety and efficacy (20).

Pharmaceuticals that control fertility are known as oral contraceptives, or antifertility drugs (2). These medications affect the menstrual cycle and female ovulation. A combination of progesterone and estrogen is commonly found in birth control pills. When a contraceptive stops women from ovulating, implantation, fertilization, zygote destruction, or abortion, it is considered effective. It also has an effect on gonadotrophin levels or sperm viability, suppresses testosterone, and stops male spermatogenesis. At the moment, many developing nations are taking action to curb population growth (21). By preventing the

production of prostaglandins, drugs like oxyphenbutazone, indomethacin, and acetylsalicylic acid have shown antifertility effects in studies involving albino male and female rabbits. In particular, indomethacin and oxyphenbutazone affect reproductive processes in male rabbits. In many developing countries, the trend of population control is common. Additionally, it has been demonstrated that the aforementioned compounds in albino rabbits decrease prostaglandin synthesis and have antifertility effects. Oxyphenbutazone and indomethacin have a significant impact on male rabbit reproductive processes (22). Because they are less toxic and have been used for a long time in traditional medical practices like Ayurveda, people are increasingly choosing plant-derived medications over synthetic ones. To encourage family planning, a variety of contraceptive methods have been promoted. However, there is now more interest in indigenous herbs for their possible contraceptive qualities due to the serious side effects linked to synthetic steroidal contraceptives. Consequently, it is essential to explore suitable native plant products that could serve as alternatives to conventional tablets (23).

In many parts of the world, such as Morocco, Saudi Arabia, Taiwan, and Trinidad and Tobago, ethnobotanical research on medicinal plants used by local populations has been carried out. Several plant species have been found to have antifertility properties. The use of plant-based remedies has long been a part of traditional medicine practices for fertility control in many parts of Ethiopia, India, and the rest of the world. Without a thorough understanding of their mechanisms, a variety of medicinal plants have been used as dietary supplements and to treat a wide range of illnesses, including infertility. A sizable fraction of these medicinal plants also show varied degrees of toxicity, even though many herbal plants have a variety of antifertility qualities, including anti-implantation, abortifacient, estrogenic, and spermicidal effects (24). Since the dawn of civilization, traditional plants have been essential to human society, helping to fight off a variety of illnesses. Historically, natural products—including plants, animals, and minerals—have been the cornerstone of disease treatment. Nearly 80% of developing countries, according to the World Health Organization, struggle to obtain synthetic drugs and must instead rely on traditional medicines, which are mostly made from plants, to meet their basic medical needs (25).

Although estrogen and progesterone-containing contraceptives are currently widely used and effective for family planning, many countries have banned the use of hormonal contraceptives due to the serious side effects of synthetic steroidal contraceptives, including gonadal toxicity, temporary or permanent infertility, testicular germ cell cancer, breast and prostate cancer, brain developmental issues, endometriosis, obesity, cholelithiasis, gastrointestinal disturbances, asthma, venous thromboembolism, and early puberty. The dangers associated with these drugs have led to research into novel compounds made from medicinal plants that could replace conventional antifertility drugs.

The objective of the current study is to review the antifertility properties of various medicinal plants.

II. Materials and Methods

The information presented in this review is the outcome of a comprehensive bibliographic investigation, which involved the analysis of classical textbooks, scientific journals, and consultation of globally recognized databases. Peer-reviewed articles were collected from various sources, including SCOPUS, PUBMED, GOOGLE SCHOLAR, and INFLIBNET.

a) Reproductive Systems

The conceptive framework is a sex organ inside a life form that works with the end goal of sexual propagation. Numerous non-living substances, for example, liquids, hormones, and pheromones, are the most significant types of gear for regenerative frameworks (26).

i. *Male Reproductive System*

The different sex organs that play a major role in human generation are part of the male conceptual framework. These organs are located inside the pelvis and outside the body. An ovum in the female's body is fertilized by the sperm and semen produced by the penis and gonads, the main male sex organs. The fertilized ovum grows into a fetus, which is subsequently born as an infant (26).

ii. *Female Reproductive System*

The inner and outer sex organs make up the female conceptual framework. It is attempting to increase the number of new generations. when the female human reproductive system matures after being immature at birth. One can produce gametes and carry a fetus to term through puberty. The ovaries, fallopian tubes, and uterus are the internal sex organs. Undeveloped organisms that develop into fetuses are called uterus or belly obliges. Additionally, the uterus produces uterine and vaginal discharges that facilitate sperm transit to the Fallopian tubes. The egg cells are made in the ovaries. Genitals and vaginal openings are other names for the external sex organs. The cervix is where the vagina and uterus are joined (26).

b) Antifertility

Antifertility agents are substances that can inhibit ovulation or fertilization, ultimately leading to the termination of a pregnancy (27). Medications designed to prevent fertilization are referred to as having antifertility effects, which are also known as contraceptive effects. Contraception encompasses

methods that disrupt the natural processes of ovulation, fertilization, and the implantation of the ovum, thereby preventing pregnancy (28).

A concise overview of plants exhibiting antifertility properties, along with their active components, is presented in *Table 1*. The investigation of various antifertility medicinal plants led to the conclusion that the efficacy of different plant parts is ranked as follows: Leaf > Seed > Whole Plant > Root > Aerial Part = Bark > Stem > Fruit = Flower > Tuber > Stem Bark > Rhizome. The leaves demonstrate the highest potential for antifertility activity, while the rhizome shows the least potential (see *Figures 1 and 2*).

c) Medicinal plants used as antifertility agents

i. *Antiovulation Activity*

Polygonum hydropiper Linn (Marsh Pepper) belongs to the family Polygonaceae, which is in part valued for its roots and leaves and adds such active ingredients as formic acid, acetic acid, beldianic acid, tannin, essential oil, and oxymethyl-anthraquinones. It is used in situations involving diarrhea, skin problems, hemorrhoids, and dyspepsia. It is used in folk medicine as an anti-cancer and anti-rheumatic agent. Biologically, these constituents can have antioxidant, antimicrobial, anti-inflammatory, and antifertility effects in humans. In one study, Kapoor *et al.* (1974) (30) have reported on the anti-ovulatory activity in this plant. Their study using three varieties of extracts (petroleum, aqueous, and alcohol) was conducted to examine the antifertility activity of this particular plant. Antifertility activity was noticed in rabbits with copper-induced ovulation. Petroleum ether extract of the roots of Polygonum hydropiper was detected adequately in inhibiting ovulation in 60% of the animals. All the other extracts prohibited ovulation in 40% or less of the animals (30).

ii. *Anti-Implantation Activity*

Ailanthus excelsa Roxb is a deciduous tree from the Simaroubaceae family and is widely distributed in Asia and northern Australia. Its native origin is China and is known as the “tree of heaven” (6). In Maharashtra, the above plants were used traditionally for anti-implantation and abortification activity *(Table 2)*. Ailanthus excelsa Roxb is a deciduous tree from the Simaroubaceae family and is widely distributed in Asia and northern Australia. Its native origin is China and is known as the “tree of heaven” (6). In Maharashtra, the above plants were used traditionally for anti-implantation and abortification activity *(Table 2)*. Ailanthus excelsa Roxb is a deciduous tree from the Simaroubaceae family and is widely distributed in Asia and northern Australia. Its native origin is China and is known as the “tree of heaven” (6). In Maharashtra, the above plants were used traditionally for anti-implantation and abortifacient activity *(Table 2)*. Ailanthus excelsa Roxb is an abscission tree from the Simaroubaceae family and is extensively distributed in Asia and northern Australia. Its ancient origin is China and is known as the “tree of heaven” (32). In Maharashtra, the above plants were used habitually for anti-implantation and abortifacient activity.

The anti-implantation activity was purposive according to the method of Olagbende-Dada Stella O *et al.*, 2009 (33). Eighteen mature, female, colony-bred Wistar albino rats were divided into three groups (6 female rats per group). One group was used as a control, and the other two groups were used as a test group. Female rats in the proestrous phase were kept with males with confirmed fertility in a ratio of 2:1. The female rats were examined in the following morning for verification of copulation; the vaginal smear was examined for thick clumps of spermatozoa. The day on which the spermatozoa were found in the smear was observed the first day of pregnancy (Day 1). A 150 mg/kg of body weight and 300 mg per kg of body weight of the extract was administrated intragastrically for 10 days from day 1 to day 10 of pregnancy for the test group and equal volume of vehicle for the control group. On day 11, all groups of rats were laparotomized under light ether anesthesia to determine the number of implantation sites in the horns of the uteri. The presence of a difference in the mean number of propagation sites between the extract and the control was taken as a positive response.

iii. *Antispermatogenic Activity*

Plumbago zeylanica belongs to the family Plumbaginaceae, and its antifertility ingredients include roots and leaves. Its active rules are plumbagin, isoshinanolone, transcinnamic acid, vanillic acid, beta-sitosterol, 4-hydroxybenzaldehyde, and plumbagic acid, and it is used to cure piles, leukoderma, and other skin diseases. It developed to foster diverse biological activities, including anti-Helicobacter pylori, antidiabetic, antioxidant, and antifertility. An earlier rat study was initiated using the plant's ethanol extract. When the applied extract dosage was 159 mg/kg, seminiferous tubule diameters became smaller, and spermatocyte and spermatid production was reduced. Furthermore, a decline in immature and mature Leydig cells occurred, and degenerating cells were significantly increased. Lastly, the testicular cell population was decreased. Overall, this study showed palpable plant-based antifertility activity (34).

iv. *Abortifacient Activity*

Plumeria rubra L. are secreting latex trees and shrubs that belong to the Apocynaceae family. The commixture of bark & roots of Plumeria rubra is traditionally used to treat asthma, ease constipation, stimulate menstruation, and reduce fever, and the latex is used to soothe irritation (35). In India, however, its fruit is used as an abortifacient (36).

The plant extracts were checked in female albino rats for abortifacient activity as per Khanna *et al.* (1969) (37). The female rats in the pro-estrous stage were caged with males of proven fertility in the ratio of 2:1 in the evening and examined the successive day for the evidence of copulation. Rats exhibiting a thick clump of spermatozoa in their vaginal smear were partitioned, and that day was designated as day 1 of pregnancy. These rats were irregularly distributed into 13 groups, one control group and 12 experimental groups of 6 animals each. On the day of pregnancy, animals were laparotomized below light ether anesthesia using sterile conditions. The two horns of uteri were inspected to determine the implantation sites. Thereafter the abdominal wound was sutured in layers (38).

d) Hormonal Control of Fertility

The birth control pill, the most effective form of birth control, is based on the oral administration of steroids. Either progestins and estrogens are used together, or progestins are used alone, as with the minipill. Furthermore, different combinations of steroids can be given intrauterine or as long-acting injectable preparations. Estradiol and progesterone are not suitable for use in oral pills because they are metabolized in the liver and gastrointestinal tract. Therefore, different synthetic progestins like norethindrone, norethindrone acetate, norgestrel, ethinodiol diacetate, or norethynodrel are used in conjunction with synthetic estrogens like mestranol or ethinyl estradiol. The hormones are administered in a cyclical manner for 21 days, starting on the fifth day of the menstrual cycle and ending with either no pills or a placebo for 7 days. Through negative feedback effects on the hypothalamus, the high levels of progestin and estrogen prevent ovulation and the midcycle LH surge. While FSH levels are typically suppressed, irregular LH peaks can occasionally be seen. Estrogens are still secreted, but ovarian progesterone production is reduced. Depending on the type and dosage of the contraceptive, the effects on the endometrium can vary. Within a few days of beginning daily intake, there is a rapid progression from proliferation to early secretory changes, which are followed by regressive changes (39).

e) Mechanism of Action of Antifertility Plants

It has been reported that medicinal plants have antifertility effects through a variety of mechanisms. Their impact on sex hormones, specifically for reducing fertility, regulating the menstrual cycle, alleviating dysmenorrhea, treating enlarged prostate, menopausal symptoms, breast pain, etc., is one of their main functions (40). Furthermore, by peripherally modulating follicle-stimulating hormone (FSH) and luteinizing hormone (LH), plants with estrogenic qualities can directly affect pituitary action, reducing their secretions and preventing ovulation (41). On the other hand, plants that have anti-estrogenic properties have abortifacient effects and interfere with the development of the ovum and endometrium (42).In females, the hypothalamus, anterior pituitary, ovary, oviduct, uterus, and vagina are the sites of action of antifertility medications. Antifertility effects primarily occur in the mammalian uterus (40). In immature rats, typical estrogenic compounds can cause cornification and vaginal opening, as well as increase the uterine wet weight, all of which have anti-implantation effects (43). When given to male rats, plant extracts have also demonstrated encouraging antifertility effects. Plants have a variety of effects on the male reproductive system that can cause antifertility, such as antispermatogenic, post-testicular, spermicidal, sperm immobilizing, and antiandrogenic effects.

f) Medicinal plants with significant antifertility activity

Although some herbal contraceptives have been developed, their potential for human use is limited. People are now searching for herbal remedies to combat a variety of illnesses and regulate fertility as a result of these issues (44). There are a number of preventive and corrective contraceptive methods available thanks to modern medicine, but none of them are particularly safe or free of major side effects. Drugs that are synthetic or chemically based have the potential to disrupt the endocrine system and have effects on the body's metabolism, development, neurological function, and reproduction. Natural hormone synthesis, secretion, transport, and activity may all be adversely affected by these substances. By preventing the synthesis and metabolism of hormones or by obstructing their action, they disrupt the normal level of hormones. Among them are Alkylphenols, bisphenol A, dioxins, heavy metals, fungicides, and insecticides prevent the synthesis of estrogen and progesterone, which impacts female sexual development by causing toxicity to the gonads, testicular germ cell cancer, breast/prostate cancer, and endometriosis. Pesticides, phthalates, and plasticizers also prevent the production of androgens, which impacts male sexual development. Other negative effects of these chemicals on the reproductive system have been demonstrated, including temporary or permanent infertility (45). These factors make it essential to create a highly effective, entirely herbal medication that doesn't negatively impact the reproductive system. Worldwide, over 35,000 plant species are utilized for medicinal purposes in a variety of human cultures. For primary healthcare, almost 80% of people worldwide rely on traditional medicines, the majority of which use plant extracts (46). People have been using plants to treat illnesses and ease physical pain since ancient times. Many traditional medicines are now recognized for their effectiveness, reduced side effects, and improved cultural acceptability and compatibility with the human body. The need for the development of safe and effective herbal contraceptives Even the savages of

ancient societies used herbal contraceptives to manage their fertility and avoid getting pregnant. Although some significant anti-fertility drugs (contraceptives) for women have been discovered by conventional medicine, their use and popularity among women are limited because of certain undesirable and problematic side effects. Obesity, cholelithiasis, stomach issues, breast and cervical cancer, asthma, and venous thromboembolism are among the frequent adverse effects (47).

Medical professionals are therefore looking for herbal contraceptives that are both safe and effective. Numerous plants have anti-fertility properties that have been scientifically proven. Both men and women may find these plants to be a useful source of herbal contraceptives. Due to their minimal or nonexistent adverse effects, plant products have caught the interest of numerous scientists as a major source of naturally occurring fertility-regulating agents. There have been reports of several plant extracts acting as antifertility agents (48). Given India's long-standing concerns about population growth, medicinal plants have been examined for their potential as contraceptives and anti-fertility effects. There are fewer options for effective, reversible, non-irritating, and highly expectable contraceptives available to men who are willing to share family planning responsibilities, and female contraceptive methods have always been given priority. Additionally, some herbs have been shown to disrupt the regular movement or production of sperm. Since every herb has a unique use, it's critical to have a basic understanding of how they are or might be used. Let's clarify the potential courses of action in more detail. Traditional herbal medicine-based sterilization techniques, such as abortion during the first few weeks, preventing conception, or rendering either partner sterile, are employed to regulate population growth rates. A review of the literature showed that, with the exception of gynecological disorders, herbal remedies that induce abortion, and plants that induce abortion, sufficient research has been done on the various medicinal uses of plants in this region (49). Numerous plant products have the potential to be developed into contraceptives by inhibiting both male and female fertility. Only a small number of native plants have been studied for their anti-fertility properties thus far, despite the fact that many of them have been demonstrated to prevent conception. The anti-fertility effects of a variety of medicinal plant extracts have been investigated in both males and females. Hormone levels were changed and spermicidal in some of these plants (50). Currently, there is a global effort to investigate the effectiveness of herbal products as a form of birth control (51).Synthetic drugs are losing ground to plant-based products. Their low toxicity and extensive exposure to these medications in traditional medical systems such as Ayurveda are the main reasons for this in recent years. Therefore, it is necessary to look for appropriate products made from local medicinal plants that can be used in place of pills. In an effort to reduce adverse effects and increase efficacy, the types and quantities of these ingredients have evolved over time (52). There are various ways that medicinal plants can cause infertility in females. In addition to interfering with implantation and sperm penetration, they may have an impact on the ovary, uterus, hormone production, and inhibition of hormonal action. Some of them create a protective layer around an egg to stop fertilization. Since antifertility plants are medications that prevent gametes from forming and disrupt the fertilization process, the plants can be categorized based on these actions. Ovulation is suppressed by antioestrogenic plants. These medications are administered by injection or by mouth. Anti-implantation plants stop fertilized ovum from attaching or penetrating the uterus. Abortifacients The fetus is expelled early by plants (53). In females, the hypothalamus, anterior pituitary, ovary, oviduct, uterus, and vagina are the sites of action of antifertility medications. By releasing follicle-stimulating hormone (FSH) and luteinizing hormone (LH), the hypothalamus regulates the uterus's activity. Therefore, antifertility drugs may work at this level by interfering with the pituitary and/or hypothalamus's hormonal function or by blocking the neural pathway to the hypothalamus that regulates the release of hormones that release gonadotropin.

Male contraceptive options and progress are still limited and slow, despite significant advancements in the development of highly effective, acceptable, and reversible methods for females (13). New methods of male contraception must be developed in light of recent advancements in our understanding of male reproductive physiology. Numerous possible methods for causing infertility have been studied for a long time, including immunological, chemical, and hormonal methods. A variety of chemical groups, including steroidal and non-steroidal ones, have an impact on testicular function. These include melatonin, α-chlorohydrin, serotonin, levonorgestrel, depot medroxyprogesterone acetate (DMPA), cyproterone acetate (CPA), Danazol, and metapiron. However, their use has failed due to a number of risks, as they have been shown to be toxic or idiosyncratic in both short- and long-term use in the reproductive organs (54). Even though there are many different forms of contraception, finding newer, more effective ones is one of the most difficult tasks in the field of pharmaceutical and medical sciences. Exploration of the hidden wealth of medicinal plants for use as contraceptives has recently begun. A large portion of the global population still has access to herbal medicine as a common form of therapy for both illness treatment and health maintenance. Information about the screening of plants with antifertility efficacy has been steadily accumulating (55). The antifertility program can benefit from the knowledge found in

folklore and ancient literature about plants and herbs. Many plants have been identified recently, and researchers have evaluated extracts and active ingredients from various plant parts, such as seeds, roots, leaves, flowers, stems, or stem barks (56).

III. Results

To investigate the traditional and folkloric uses of plants with antifertility properties, a thorough analysis of a large number of scientific peer-reviewed publications was carried out. Several plants that have been asserted and proven to have antifertility properties were included in the study. A list of plants that have been shown to have antifertility properties is provided below, along with information on the precise parts used and how they work.

IV. Discussion

Medicinal plants have been utilized for their therapeutic properties throughout history across various regions of the globe. In India and other countries, numerous medicinal plants are documented to exhibit antifertility effects (57).

This review aims to provide a comprehensive analysis of ethnopharmacological data concerning plant species utilized for the regulation of fertilization and conception by various tribes worldwide over recent decades. *Table 3* includes the names of these plants, along with their respective families, the parts used, the animal models employed, and their mechanisms of action. As indicated in *Table 3,* the plants are categorized based on their effects as antifertility agents, with some exhibiting multiple properties that vary according to dosage. Furthermore, this review presents a compilation of plants that play a significant role in fertility control for both males and females. The literature survey revealed that among the different parts of plants, leaves are predominantly used for the purpose of controlling fertilization, while other parts such as fruits, stems, bark, roots, seeds, and flowers are utilized in lesser amounts (58).

V. Conclusion

To sum up, this review has brought together data that has been verified by science about the phytochemical components and antifertility properties of medicinal plants that have been used for centuries. The results show that these medicinal plants' extracts have strong antifertility effects. Additionally, the findings show that the previously mentioned plants have dose-dependent antifertility effects.

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Table 1: List of Antifertility Plants with Chemical Constituents (29)

S.No.	Plant name	Common name	Type of extract	Plant part used	Activities	Chemical Constituents
1.	*Abrus precatorius*	Chirmi	Methanolic	Seed	Antifertility	Precatorine, trigonelline, choline, abrine abricin, abridin
2.	*Acacia catechu*	Katha	_	Exudate	Anti-implantation	_
3.	*A. leucophloea*	Reonja	Alcoholic	Root	Antifertility	Tannins, flavonoids, terpenes, alkaloids
4.	*Acacia nilotica*	Babul	Aqueous	Pod	Antispermatogenic	Phytosterols, phenolic compounds, saponins
5.	*Azadirachta indica*	Khokli	Petroleum ether and ethanolic	Whole plant	Post-coital activity	β-Sitosterol, acalyphine, triacetonamine, kaempferol, tannin, stigmastrol
6.	*Achyranthus aspera*	Chirchira	Ethanolic	Root	Anti-implantation	Ecdysterone, oleanolic acid, n-hexacos-14-enoic acid
7.	*Adathoda vasica*	Arusa	_	Leaves	Anti-iplantation	Vasicine
8.	*Aegle marmelos*	Bael	Ethanolic	Leaves	Antifertility	Alkaloids, caumarins, steroids
9.	*Aerva lanata*	Bui	Ethanolic	Root	Anti-implantation	Alkaloids, kaempferol, quercetin, β-sitosteryl acetate, tannic acid
10.	*Albizzia lebbek*	Siris	Methanolic	Pod	Spermicidal activity	Lebbekanin-E
11.	*Ammanaia baccifera*	Aginbuti	Ethanolic	Whole plant	Antisteroidogenic	Steroids, triterpenoids, Flavonoids, and tannins
12.	*Amaranthus spinosus*	Kanta chaulai	Acetone	Root	Anti-spermatogenic and anti- androgenic	Alkaloids, flavonoids, saponins, β-sitosterol, stigmasterol, Kaempferol, glycosides
13.	*Amaramthu viridis*	Jangli cholai	Aqueous	Root	Abortifacient	Alkaloids, anthraquinon, saponins
14.	*Anagallis arvensis*	Dhartidhak	_	Whole plant	Spermicidal activity	Oleanolic acid
15.	*Andrographis paniculate*	Kiryat	Dry leaf powder	Leaves	Antispermatogenic	Flavonoids, andrographilode, diterpenoids, phenylpropanoids, oleanolic acid, and β-sitosterol
16.	*Aristolochia indica*	Indian Birthwort	Ethanolic	Root	Antispermatogenic/ anti-androgenic	Aristolic acid, p-coumric acid, methyl aristolate
17.	*Argemone maxicana*	Satyanashi	-	Seed	Anti-spermatogenic	Isoquinoline alkaloids, dihydro palmatine hydroxide, berberine, protopine
18.	*Azardirachta indica*	Neem	Alcoholic	Flower	Antifertility	Steroids, triterpenoids, alkaloids, phenolic compound, flavonoids
19.	*Balanites aegyptiaca*	Desert date	Methanolic	Bark	Antiimlantation	β-sitosterol, bergaptem, marmesin, β-sitosterol glucoside
20.	*Balanites roxburghii*	Desert date	Ethanolic	Fruit	Abortifacient	Alkaloids, saponins, tannins, flavonoids, phenolic compound
21.	*Bbiophytum sensitivum*	Lakshmana	Ethanolic	Whole plant	Antifertility activity	Phenolic and polyphenolic compound, saponins
22.	*Boerhavia diffusa*	Khapra-ara	Methanolic	Root	Antiimplantation, antiestrogenic	β-sitosterol, alkaloids, ursolic acid
23.	*Butea monosperma*	Dhak	Petroleum ether and Chloroform	Root	Anti-steroidogenic	Glycine, glycoside, aromatic hydroxyl compound
24.	*Cajanus cajan (L)*	Arhar	Methanolic	Seed	Antifertility	Sitosterol
25.	*Calotropis gigantea*	Madar	Ethanolic	Root	Anti-implantation	Akundarin, calotropin
26.	*Calotropis*	Aak	Ethanolic	Root	Anti-implantation	Alkaloids, flavonoids, tannins,

	procera					saponins, and cardiac glycosides
27.	*Capparis decidua (aphylla)*	Kair	Ethanolic	Whole plant	Antispermatogenic	Capparin, capparilin, capparinin, sitosterol, n-triacontanol
28.	*Cassia fistula*	Amaltash	Aqueous	Seed	Antiestrogenic	Anthraquinone, glycosides, flavonoids, phenolic compound
29.	*Cassia occidentalis*	Kajondi	Ethanolic	Root	Anti-implantation and abortifacient	β-sitosterol, campesterol, emodin, 1,8-dihydoxyanthraquinone, quercetin
30.	*Celsia cromandeliana*	Kokhima	Methanolic	Arial part	Antiovulatory	_
31.	*Convolvulus arvensis*	Field bindweed	Alcoholic	Arial part	Antispermatogenic	α-amyrin, campesterol, stigmasterol, β-sitosterol, quercetin, kaemferol, p-caumaric acid
32.	*Corchorus olitorius*	Nalta jute	Methanolic	Seed	Antisteroidogenic	Hydrocyanin, cardiac glycosides, tannins, flavonoids, anthraquinones, saponins, Corchoroside A, helveticoside, coroloside, digitoxigenin, periplogenin
33.	*Cordia dichotoma*	Lasora	Methanolic	Bark	Antiimplantation	α-amyrins, lupeol-3-rhamnoside, β-sitosterol, β-sitosterol-3-glucoside, toxifolin-3,5-dirhmnoside
34.	*Crotolaria juncea*	Sunnhemp	Petroleum ether, Benzene and ethanol	Seed	Antispermatogenic	Flavonoids, alkaloids, saponins, volatile oil
35.	*Cuscuta reflexa*	Amarbel	Methamolic	Stem	Anti steroidogeic	Kaemferol-3-o-glucoside quercetin, quercetin-3-0-glucoside
36.	*dactylon*	Durva	Aqueous	Whole plant	Anti-implantation	Flavonoids, tannins, phenolic compound
37.	*Cyperus rotundus*	Nut grass	_	Tuber	Antifertility	Tannins, flavonoids, coumarins, sterols
38.	*Dactyloctenium aegypticum*	Crowfoot grass	Ethanolic	Whole plant	Antifertility activity	Saponins, flavonoids, tannins, terpenoids, alkaloids
39.	*Dalbergia sisso*	Seesam	Ethanolic	Stem bark	Anti-spermatogenic	Isoflavones, flavone, β-amyrin, β-sitosterol, stigmasterol
40.	*Datura metal*	Datura	Acetone	Seed	antifertility	Saponins, flavonoids, tannins, glycosides, alkaloids, terpenoids
41.	*Dendrophthoe falcata*	Banda	Methanolic	Stem	Depression of spermatogenesis	β-amyrin-6-acetate, oleonolic acid, β-sitosterol, stigmasterol
42.	*Dolichos biflorus*	Kulattha	Acetone	Seed	Anti spermatogenic antiandrogenic	Isoflavone diglycoside, aglycone
43.	*Emblica officinalis*	Amala		Fruit	Abortifacient	
44.	*Feronia limonia*	Wood apple	Ethanolic	Fruit pulp	Antispermatogenic	Polyphenols, phytosterols, saponins, tannin, coumarins, Triterpenoids
45.	*Ficus benghalensis*	Bargad	Ethanolic	Leaves	Suppression of the spermatogenesis	Tannins, flavonoids, steroids
46.	*Ficus religiosa*	Peepal	_	Fruit	Anti-implantation	n-hexadecanoic acid, 9,12-oct-adecadienoic acid, 9,12,15-octade-catrienoic acid, butyl 9,12,15-oct-adecatrienoat
47.	*Gnaphalium indicum*	Cudweed	Ethanolic	Whole plant	Anti-implantation	Luteolin, quercetin, quercetin-3- methyl ether
48.	*Grangea maderaspatana*	Mukhatari	Flavonoid extract	Whole plant	Anti-implantation	Sesquiterpenoids, γ-gurjunene, terpinyl acetate, hinesol
49.	*Ipomoea fistulosa*	Pink morning glory	Alcoholic	Plant without root	Postcoital antifertility	Alkaloids, glycosides, phenolics, tannins, phytosterols, flavonoids, saponins
50.	*Mangifera indica*	Mango	Methanolic	Leaves	Antispermatogenic	Saponin, anthraquinone, steroids, tannin, flavonoids
51.	*Maytenus emarginate*	Kankero	Methanolic	Leaves	Inhibition of spermatogenesis	Tannins, flavonoids, alkaloids, steroids
52.	*Melia azedarach*	Chinaberry	_	Seed	Abortifacient	Alkaloids, tannins, saponins, phenols, glycosides, steroids, terpenoids, flavonoids
53.	*Mimosa pudica*	Touch me not	_	Root	Contraception and abortion	Alkaloids, glycosides, steroids, flavonoids, phenols
54.	*Nelumbo nucifera*	Lotus	Ethanolic	Seed	Antiestrogenic	Alkaloids, flavonoids, ursane triterpenoid ester
55.	*Nyctanthes arbortristis*	Har singar	Methanolic	Stem bark	Antispermatogenic	Alkaloid, phytosterols, phenolics, tannins, flavonoids, saponins
56.	*Ocimum*	Shyam Tulsi	Hydroalcoholic	Leaves	Antifertility	Saponins, glucosides, alkaloids,

	basilicum					tannins, and phenolic compounds
57.	*Opuntia dillenii*	Naagfani	Methanolic	Phylloclade	Antispermatogenic	Vitexin, isorhamnetin
58.	*Purgularia deamia*	Sagovani	Ethanolic	Stem, leaves	Antifertility	Flavonoids, terpenoids, steroids, alkaloids
59.	*Polygonum glabrum*	Neli	_	Root	Contraceptive	Sterol
60.	*Portulaca oleracea*	Purslane	Petroleum ether, chloroform, and ethanol crude	Arial part	Abortifacient	Alkaloids, tannins, flavonoids, saponins, and triterpenoids
61.	*Rivea hypocrateriform*	Night glory	Ethanolic	Arial part	Antiovulatory	Alkaloids, glycosides, saponins, tannins, phenolic compound
62.	*Salvadora persic*	Meswak	Aqueous	Leaf and stem	Antifertility	Octacosanol, 1-triacantanol, β-sitosterol, β-sitosterol-3-o-β-D-glycopyranoside
63.	*Sida acuta*	*common* wireweed	Ethanolic	Leaf	Antiimplantation	Alkaloids, steroids, glycosides, saponins, flavones, phenolic compound
64.	*Syzygium cumini*	Jamun	Alcoholic	Seed	Antispermatogenic	β-pinene, terpinolene, eugenol, rutin, quercetin,β-sitosterol
65.	*Terminalia bellirica*	Harad	Ethanolic	Bark	Anti-implantation	Phytosterols, flavonoids, phenolic comp., tannins
66.	*Terminalia chebula*	Harad	Acetone, Methanol, Ethanol, Aqueous	Bark	Antispermatogenic	Tannins, flavonoids, sterolstriterpenoids
67.	*Tactona grandis*	Teak	Petroleum ether	Stem	Antifertility	Lapachol
68.	*Tamarindus indica*	Imli	_	Fruit	abortifacient	_
69.	*Tephrosia purpurea*	Unhali	_	Seed	Purpurin, rutin	_
70.	*Terminalia arjuna*	Arjun tree	_	Bark	Antiimplantation, Abortifacient	Lupeol, oleanolic acid, arjunic acid, arjunetin, arjunolitin
71.	*Tinospora cordifolia*	Giloya	Methanolic	Stem	Antifertility	Alkaloids, sesquiterpenoid, β-sitosterol, cordifolia, columbin
72.	*Tribulus terrestris*	Gokhru	_	Seed	Abortifacient	Alkaloids, flavonoids, saponins, tannins
73.	*Vicoa indica*	Banjhauri	_	Plant	Antiimplantation	Vicolid B, Vicolid D
74.	*Wrightia tinctorial*	Duhi	Ethanolic	Stem bark	Post-coital interceptive avtivity	Lupeol, stigmasterol, campesterol
75.	*Zizyphus mauritiana*	Ber	Aqueous, methanolic	Bark	Spermicidal	Mauritine A, B, oleononic acid, betulonic acid

Table 2: List of Antifertility Medicinal Plants (31)

lant	Type	Dose/Body weight (mg/kg)	Activity
Cichorium intybus	50% ethanolic extract	50	Anti-implantation
Cuscuta reflexa	Ethanolic extract	800	Anti-implantation
Rubia cordifolia	Ethanolic extract	250	Anti-implantation
Urtica diocia	Ethanolic extract	250	Anti-implantation
Abroma augusta	Petroleum ether	50	Anti-implantation
Curcuma longa	Petroleum ether	200	Anti-implantation
Plumbago rosea	Acetone extract	200	Anti-implantation
Aloe barbadensis	Aqueous extract	100	Anti-implantation
Abutilon indicum	50% aqueous methanolic extract	500	Anti-implantation
Artemisia vulgaris	Methanlic extract	300 and 600	Anti-implantation

Table 3: List of Medicinal Plants Reported to Possess Antifertility Effects (58)

S. no.	Name of the plant	Family	Part used	Animal model	Mechanism of action
1.	*Abroma angusta* Linn.	Sterculiaceae	Roots	Rat	Antiimplantation & Abortifacient
2.	*Abrus precatorius* Linn.	Fabaceae	Seeds	Rat	Reduced sperm motility, Post-testicular antifertility effect
3.	*Acacia auriculaeformis* A. Cunn.	Fabaceae	-	-	Sperm immobilizing effect
4.	*Acacia caesia* Wight & Arn	Leguminosae	Fruit	-	Immobilization of spermatozoa
5.	*Acacia concinna* DC	Fabaceae	Stem bark	Rat	Spermicidal and semen coagulating activities
6.	*Acalypha indica* Linn.	Euphorbiaceae	Whole plant	-	Anti-estrogenic activity
7.	*Achillea millefolium* Linn.	Asteraceae	Flowers	Mice	Antispermatogenic effect
8.	*Achyranthus aspera* Linn.	Amranthaceae	Root	Rat	Spermicidal action
9.	*Actiniopteris dichotoma* Kuhn	Pteridaceae	Whole plant	Rat	Antifertility effect
10.	*Adhatoda vasica Nees Syn. Justice adhatoda L.*	Acanthaceae	Leaves	Rat	Antiimplantation & Abortifacient
11.	*Aegle marmelos* Corr. Ex Roxb.	Rutaceae	Leaf	Rat	Resist process of spermatogenesis and decrease sperm motility
12.	*Aerva lanata* (L.) Juss. Ex. Shult	Amaranthaceae	Aerial parts	Rat	Antiimplantation effect
13.	*Afromosia laxiflora* (Baker) Harms	Fabaceae	Stem bark	Rat	Antigonadotropic activity and blocks oestrous cycle
14.	*Ailanthus excelsa* Roxb.	Simaroubaceae	Leaf, Stem, Bark	Rat	Antiimplantation effect and Early Abortifacient
15.	*Alangium Salvifolium* (L.f.)	Alangiaceae	Stem, Bark	Rat	Antiimplantation & Abortifacient
16.	*Albizia procera* (Roxb.) Benth.	Leguminosae	Seed and Root	Rat	Spermicidal and semen coagulating activities
17.	*Albizia lebbek* (Linn.) Benth.	Mimosacaeae	Pod, Bark	Rat	Antifertility activity
18.	*Allium cepa* Linn.	Liliaceae	Bulb	Rat	Antiimplantation activity
19.	*Allium sativum* Linn.	Amaryllidaceae	Pod	Rat	Antispermatogenic activity
20.	*Aloe barbadensis Mill. Syn. Acalypha indica, A. litoralis, A. vera*	Liliaceae	Leaves	Dog	Antiandrogenic activity
21.	*Alstonia scholaris* R.Br.	Apocynaceae	Stem bark	Rat	Antifertility activity
22.	*Amaranthus spinous* Linn.	Amaranthaceae	Root	Rat	Inhibit fusion of Sperm and Ovum
23.	*Amaranthus viridis* L.	Amaranthaceae	Root	Rat	Contraception Activity
24.	*Anacardium occidentale* Linn.	Anacardiaceae	Nut Shell	Rat	Spermicidal
25.	*Anagalis arvensis* Linn.	Primulaceae	Whole Plant	Rat	Spermicidal and semen coagulating activities
26.	*Ananas comosus* Merr.	Bromeliaceae	Unripe fruit	Rat	Antispermatogenic activity
27.	*Andrographis paniculata* Wall. Ex Nees	Acanthaceae	Leaves	Rat	Antispermatogenic and antiandrogenic
28.	*Arctium lappa* Linn.	Asteraceae	Leaves and roots	Rat	Abortifacient
29.	*Ardisia solanacea* Roxb.	Myrsinacea	Plants excluding roots	Rat	Spermicidal Activity
30.	*Aristolochia indica* Linn.	Aristolochiaceae	Root	Presbytes langur	Antispermatogenic and antiandrogenic
31.	*Artemisia afra* Jacq. Ex Wild.	Asteraceae	Leaf	Rats	Abortion
32.	*Artemisia vulgaris* Linn.	Asteraceae	Leaves	Rats	Antiimplantation and Estrogenic activity
33.	*Aspilia Africana* (pers.) C.D. Adams	Asteraceae	Leaves	Rats	Antiovulatory Activity
34.	*Austroplenckia populnea* (Reiss.) Lundell.	Celastraceae	Pods	Rats	Affects the sexual behavior and epididymal sperm concentration
35.	*Azardirachta indica* A. Juss.	Maliaceae	Seed Oil	Rats	Antispermatogenic and antiandrogenic
36.	*Bacopa monnieri* (L.) Pennell	Scrophulariaceae	Whole plant	Rats	Contraception Activity
37.	*Balanites roxburghii* Linn.	Zygophyllaceae	Fruits	Dog	Antispermatogenic activity and testicular necrosis and atrophy

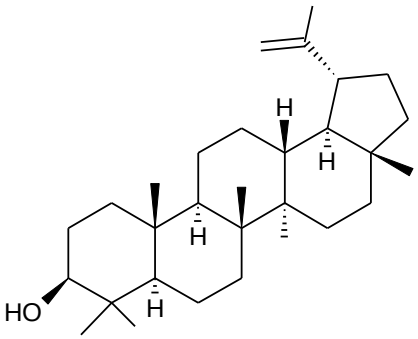
38.	*Ballota undulate* (Sieber ex. Fresen.) Benth.	Labiatae	Leaves, Flowers	Rats	Antiimplantation activity
39.	*Bambusa arundinacea* Willd.	Graminae	Shoots, Stem	Rats	Impaired the structural and functional activity of epididymis, Reduced sperm motility
40.	*Barleria prionitis* Linn.	Acanthaceae	Roots	Rat	Antifertility effect
41.	*Berberis chitria* Buch.-Ham.ex Lindl.	Berberidaceae	Root	Dog	Antispermatogenic activity
42.	*Biophytum sensitivum* (L.) DC.	Oxalidaceae	Leaves	Rats	Antiimplantation Activity
43.	*Bougainvillea* Comm. Ex Juss.	Nyctaginaceae	Leaves	Rats	Antifertility effect
44.	*Butea monosperma* (Lam.) Kuntze	Fabaceae	Seed	Rat, Dog	Effects on testicular function
45.	*Calotropis procera* (Ait.) R. Br.	Asclepiadaceae	Roots	Rabbit, Mice	Antispermatogenic effect anf leydig cell atrophy Functional alteration in the genital organs and inhibition of fertility
46.	*Cananga odorata* (Lam.) Hook. F. & Thomson	Annonaceae	Root, Bark	Rat	Spermicidal Activity
47.	*Cannabis sativa* Linn.	Cannabaceae	Leaves	Presbytis Monkey	Testicular lesions and atrophy of Leydig cells
48.	*Cardiospermum Helicacabum* L.	Spindaceae	Whole plant	Rat	Antiimplantation activity
49.	*Carica papaya* Linn.	Caricaceae	Fruit	Rat	Antispermatogenic activity
50.	*Carum carvi* Linn.	Apiaceae	Rhizome	Rat	Antioestrogenic activity
51.	*Cassis fistula* Linn.	Caesalpiniaceae	Pods, Seeds	Rat	Antioestrogenic activity
52.	*Catharanthus roseus* G. Don syn. Vinca rosea Linn.	Apocynaceae	Leaves	Mice	Antioestrogenic activity
53.	*Celastrus paniculatus* Willd.	Celastraceae	Seeds	Rat	Antispermatogenic action
54.	*Cicer arietinum* Linn.	Fabaceae	Seeds	Rat	Abortifacient and estrogenic activity
55.	*Cichorium intybus* Linn.	Asteraceae	Whole plant	Rat	Antispermatogenic activity
56.	*Cinnamomum*	Lauraceae	Seed	Sparrow	Arrest and inhibition of spermatogenesis
57.	*Camphora* Nees & Eberm.				
58.	*Cissampelos pareira* Linn.	Menispermaceae	Leaves	Mice	Antioestrogenic activity
59.	*Citrullus colocynthis* Schrad.	Cucurbitaceae	Fruit, Root	Rat	Induced reversible antifertility effects and Antispermatogenic effect
60.	*Clerodendrum serratum* L.	Lamiaceae/Verbenaceae	Whole plant (Excluding Roots)	Rats	Spermicidal activity
61.	*Cnidoscolous aconitifolius* (Mill.)I.M.Johnst.	Euphorbiaceae	Leaves	Rats	Contraception
62.	*Cola nitida* Schott & Endl.	Sterculiaceae	Stem Bark	Rats	Antigonadotropic activity and
63.	*Colebrookia oppositifolia* Sm.	Lamiaceae	Leaf	Rats	Antifertility Effect
64.	*Combretodendron macrocarpum* (P.Beauv.) Keay	Barringtoniaceae	Stem bark	Rats	Antigonadotropic activity and
65.	*Convolvulus miicrophyllus* Sieb. ex Spreng	Convolvulaceae	Whole Plant	Rat	Antispermatogenic effect
66.	*Crataeva nurvala* Buch.Ham.	Capparidaceae	Stem Bark	Rat	Antiimplantation and Antioestrogenic activity
67.	*Crotalaria juncea* Linn.	Papilionaceae	Seeds	Mice	Antifertility Activity, Arrest of spermatogenesis and antiandrogenic Effect
68.	*Croton roxburghii* Balak.	Euphorbiaceae	Bark	Mouse	Anti-steroidogenic activity
69.	*Cumftiga racemosa* L.	Apocyanaceae	Root	Rats	Spermatogenesis
70.	*Cuminum cyminum* Linn.	Apiaceae	Seed	Rat	Antispermatogenic effect
71.	*Curcuma aromatica* Salisb.	Zingiberaceae	Rhizome	Rats	Antifertility Activity
72.	*Curcuma longa* Linn.	Zingiberaceae	Root	Rats	Interference with Spermatogenesis
73.	*Cyclamen persicum* Mill.	Primulaceae	Whole Plant	-	Spermicidal activity
74.	*Cyclea burmanni* Miers	Menispermaceae	Roots	Rat	Decrease Sperm Count
75.	*Cynomorum coccineum* Linn.	Cynomoraceae	Inner pulp of stem and root	Rats	Effect on epididymal sperm pattern
76.	*Daucus Carota* Linn.	Apiaceae	Seeds	Rat	Blastocystotoxic and Antiimplantaion effects; Postcoital contraceptive effects
77.	*Dendrophthoe falcate* (Linn. f.)	Loranthaceae	Aerial parts	Rats	Antifertility effect

78.	*Derris brevipes* Baker.	Fabaceae	Root Powder	Rats	Abortifacient
79.	*Desmodium gangeticum* DC.	Fabaceae	Whole plant	Rat	Antifertility effect
80.	*Dioscorrea bulbifera* L.	Dioscoreaceae	Tuber	-	Contraceptive
81.	*Diploclisia echinatus* Linn.	Asteraceae	Stem	-	Spermicidal
82.	*Dipsacus mitis* D.Don	Spindaceae	Root	Hamster	Contraceptive
83.	*Ecballium elaterium* A. Rich.	Cucurbitaceae	-	Rabbit	Decreases sperm motility
84.	*Echeveria gibbiflora* DC	Crassulaceae	Whole plant	Guinea Pig	Decreased sperm motility
85.	*Echinops echinatus* Roxb.	Asteraceae	Root	Rat	Sperm antimotility
86.	*Embelia Ribes* Burm.f.	Myrsinaceae	Berry	Rat	Antifertility activity
87.	*Epilobium angustifolium* Linn.	Onagrariaceae	-	Rat	Reduction in weight of accessory sex organs
88.	*Eupatorium odoratum* Linn.	Asteraceae	-	-	Spermicidal activity
89.	*Euphorbia neriifolia* Linn.	Euphorbiaceae	Root	Rat	Antispermatogenic effects
90.	*Eugenia jambolana* L.	Myrtaceae	Flowers	Rat	Antifertility effect
91.	*Ehretia cymosa* Thonn.	Boraginaceae	Leaf, Bark	-	Contraceptive
92.	*Eleutherine bulbosa* Urb.	Iridaceae	Bulb	Rat	Abortifacient
93.	*Fevillea passiflora* Vell.	Cucurbitaceae	Seed	-	Abortifacient
94.	*Ferula assa-foetida* Linn.	Apiaceae	Resin	-	Emmenagogue
95.	*Ficus religosa* Linn.	Moraceae	Fruit	Goat	Anti-implantation
96.	*Ficus wassa* Roxb.	Moraceae	Root	-	Contraceptive
97.	*Flagellaria indica* Linn.	Flagellariaceae	Leaf	-	Contraceptive
98.	*Flemingia strobilifera* (L.) J. St. Hil syn. Moghania strobilifera (L.) J. St.-Hill.	Fabaceae	Seed	-	Contraceptive
99.	*Fleura aestuans* Linn.	Utricaceae	Root	-	Abortifacient
100.	*Foeniculum vulgare* Mill.	Apiaceae	Seed	Rat	Sperm toxic
101.	*Fragaria vesca* Linn.	Rosaceae	Leaf	-	-
102.	*Franseria artemisiodes Willd.*	Asteraceae	Whole plant	-	Contraceptive
103.	*Galium mexicanum* Var.	Rubiaceae	Leaves	Cat	Abortifacient
104.	*Garcinia cambogia* Desr.	Clusiaceae	Fruit	Rat	Testicular atrophy
105.	*Gardenia jasminoides* Ellis.	Rubiaceae	Fruits	-	Abortifacient
106.	*Gloriosa superb* Linn.	Liliaceae	Roots	Rat, mice	Oxytocic activity, Abortifacient
107.	*Glossocardia bosvallia* DC.	Asteraceae	Whole plant	-	Emmenagogue
108.	*Glycyrrhiza glabra* Linn.	Fabaceae	Root	-	Emmenagogue
109.	*Gossypium barbadense* Linn.	Malvaceae	Cotton Seed	rat	Testicular
110.	*Grewia colunnaris* Sm.	Triliaceae	Root	-	Sterilizer
111.	*Hagenia abyssinica* .syn. Brayera anthalmintica	Rosaceae	-	-	Abortifacient
112.	*Haematoxylon campechianum* L.	Fabaceae	Whole plant	-	Abortifacient
113.	*Hamelia erecta* Jacq	Rubiaceae	Leaf	-	Abortifacient
114.	*Hedeoma pulegoides* Linn.	Labiateae	Plant without root	-	Contraceptive and Abortifacient
115.	*Hedera helix* Linn.	Araliaceae	Fruit	-	Contraceptive
116.	*Hibiscus rosa-sinensis* Linn.	Malvaceae	Root	Rats & Mice	Anti-implantation & Uterotropic activity
117.	*Hyptis suaveolens* Poit.	Labiatae	Whole plant	Mice	Antifertility
118.	*Hypochoeris brasiliensis* (Less.) Benth	Asteraceae	Leaf & Root	-	Contraceptive
119.	*Hypericum chinensis* Linn.	Clusiaceae	Leaf	-	Emmenagogue
120.	*Hymenaea stigonocarpa* Mart. Ex Hayne	Fabaceae	Bark	-	Contraceptive
121.	*Indigofera linnaei Ali*	Fabaceae	Herb	rats	Anti-fertility activity
122.	*Jacaranda copaia* (Aublet.) D. Don	Bignoniaceae	Tuber	-	Contraceptive
123.	*Jasminum multiflorum* (Burm.f.) Andrews	Oleaceae	-	-	Emmenagogue
124.	*Jodinia rhombifolia* (Hook. & Arn.) Reissek.	Santalaceae	Leaf	-	Abortifacient
125.	*Juglans regia* Linn.	Juglandaceae	Leaf	-	Contraceptive
126.	*Juniperus communis* Linn.	Cupressaceae	Stem & Fruit	-	Anti-implantation activity
127.	*Juniperus oxycedrus* Linn.	Cupressaceae	Berry	-	Abortifacient
128.	*Justicia simplex* D. Don	Acanthaceae	Root	-	Contraceptive
129.	*Kopsia* SP	Apocynaceae	Leaf	-	Contraceptive
130.	*Laurus nobilis* Linn.	Lauraceae	Leaf	Rats	Testicular dysfunction

131.	*Lawsonia inermis* Linn. syn. L. alba	Lythraceae	Leaves	rats	Abortifacient
132.	*Leonotis nepetaefolia* R.Br.	Labiatae	Leaf	Rats	Anti-implantation
133.	*Lepidium meyenii* Walp.	Brassicaceae	Root	Rats	invigorates spermatogenesis in male rats
134.	*Lepidium sativum* Linn.	Brassicaceae	Herb	-	Abortifacient & Anti-Ovulatory
135.	*Licuala* SP.	Arecaceae	Root bark	-	Contraceptive
136.	*Ligusticum porter* Coult. And Rose	Apiaceae	Root	-	Emmenagogue
137.	*Lithospermum officinale* Linn.	Broaginaceae	Leaves	Rat	Inhibition of hypophyseal hormone secretion
138.	*Lobelia nicotianifolia* Heyne	Campanulaceae	Whole plant	-	Contraceptive
139.	*Lonicera ciliosa*	Caprifoliaceae	Leaf	-	Contraceptive
140.	*Malvaviscus conzattii* Greenm	Malvaceae	Flower	Albino Mice	Antifertility activity
141.	*Martynia annua* Linn.	Martyniaccae	Root	Rats	Antifertility Effect
142.	*Melodinus fusiformis* Champ. Ex Benth.	Apocynaceae	-	-	Spermicidal Effect
143.	*Mentha arvensis* Linn.	Labiatae	Leaves	Rabbits	Anti-Ovulatory
144.	*Millettia auriculata* Baker. ex, Brand.	Fabaceae	Leaves	Rat	Anti-Implantation effect
145.	*Momordica charantia* Linn.	Cucurbitaceae	Seeds	Rats	Antispermatogenic
146.	*Mondia whiteii* Skeels	Apocynaceae	Root bark	Rat	Antispermatogenic & Anti fertility activities
147.	*Mucuna urens* Medik.	Fabaceae	Seed	Rat	Antispermatogenic
148.	*Myristica fragrans* Houtt	Myristiacaceae	Seed	-	Abortifacient
149.	*Mesua ferrea* Linn.	Clusiaceae	Flowers	Rat	Anti-implantation
150.	*Nardostachys jatamansi* DC.	Valerianaceae	Root	-	Emmenagogue
151.	*Nasturtium officinalis* R.Br.	Brassicaceae	Whole Plant	-	Abortifacient
152.	*Nerium indicum* Mill.	Aocynaceae	Whole Plant	-	Emmenagogue
153.	*Nicotiana tabacum* Linn.	Solanaceae	Leaves	Rat	Antiandrogenic effects
154.	*Nigella sativa* Linn.	Ranunculaceae	Seeds	Rat	Post-Coital Antifertility effect
155.	*Nothocnide repanda* (Bl.) Bl.	Utricaceae	Leaf	-	Abortifacient
156.	*Ochna jabotapita* Linn.	Ochnaceae	Plant (Without	-	Semen coagulating activity
157.	*Ocimum sanctum* Linn.	Labiatae	Leaves	Rats	Antiandrogenic Property
158.	*Olea europea* Linn.	Oleaceae	Fruit	Rats	Contraceptive
159.	*Ophiopogon intermedius* (D.Don) Maxim	Asparagaceaea	Rhizomes	-	Spermicidal
160.	*Opuntia dilleni* Haw.	Cactaceae	Phylloclade	Rats	Spermatotoxic
161.	*Origanum vulgare* Linn.	Labiatae	-	-	Abortifacient
162.	*Oxalis physocalyx* Zucc.ex Progel	Oxalidaceae	Whole Plant	-	Abortifacient
163.	*Oxytenanthera abyssinica* Munero	Poaceae	Leaf	-	Abortifacient
164.	*Papaver somniferum* Linn.	Papaveraceae	Fruit	-	Induces Abortion
165.	*Peganum harmala* Linn.	Zygophyllaceae	Epigeal Plants	Rats	Abortifacient
166.	*Petrocarpus santalinus* Linn.f.	Fabaceae	Stem Bark	Rats	Anti-implantation activity
167.	*Piper longum* Linn.	Piperaceae	Fruit	Rats	Antifertility Activity
168.	*Pittosporum neelgherrense* Wight & Arn.	Pittosporaceae	Plant (Without Root)	Rats	Spermicidal and Semen Coagulation
169.	*Plumbago zeylanica* Linn.	Plumbaginaceae	Leaves & Root	Rats	oestrogenic activity
170.	*Plumeria rubra* Linn.	Apocynaceae	Pod Extract	Rats	Anti-implantation activity
171.	*Polemonium caeruleum* Linn.	Polemoniaceae	-	-	Antispermatogenic effect
172.	*Primula vulgaris* Huds.	Primulaceae	-	-	Spermicidal effect
173.	*Pueraria tuberose* DC.	Fabaceae	Tubers	Rats	Antifertility activity
174.	*Portulaca oleracea* Linn.	Portulacaceae	Seed	Mice	Impairement of Spermatogenesis
175.	*Pyrus cuspidata* Bertol	Rosaceae	Whole Plant	-	Spermicidal effect
176.	*Quassia amara* Linn.	Simaroubaceae	Stem wood	Rats	Antifertility activity
177.	*Randia dumetorum* Lamk.	Rubiaceae	-	-	Anti-implantation effect
178.	*Randia spinosa* (Thumb.) Bl.	Rubiaceae	Fruit	-	Antifertility activity
179.	*Ranunculus sceleratus* Linn.	Ranunculaceae	Whole Plant	-	Antifertility activity
180.	*Rauwolfia serpentine* Benth.	Apocynaceae	Root	-	Antifertility activity
181.	*Rhamnus catharticus* Linn.	Rhamnaceae	-	-	Emmenagogue
182.	*Ricinus communis* Linn.	Euphorbiaceae	Seed	Guinea Pigs	Anti-implantation and Abortifacient
183.	*Rubia cordifolia* Linn.	Rubiaceae	Root	-	Antifertility activity
184.	*Rubus ellipticus* Sm.	Rosaceae	Leaves	Rats	Anti-implantation Effect

185.	*Ruta angustifolia* Linn.	Rutaceae	Leaf	-	Antifertility activity
186.	*Ruta graveolens* Linn.	Rutaceae	Aerial parts and Roots	Rats and hamsters	Anticonceptive activity
187.	*Salvia fruticosa* Mill.	Labiatae	Leaves	Rats	Anti-implantation Effect
188.	*Samida rosea* Sims.	Flacourtiaceae	Leaf	Rats	Abortifacient and Emmenagogue
189.	*Santalum album* Linn.	Santalaceae	Whole Plant	-	Abortifacient
190.	*Sapindus mukorossi* Gacrtn	Sapindaceae	Fruit Pericarp	Rats	Alteration in Sperm membrane physiology
191.	*Sarcostemma acidum* (Roxb) Voigt	Apocynaceae	Stem	Rats	Arrests Spermatogenesis
192.	*Scilla indica* (Baker)	Liliaceae	Bulb	-	Emmenagogue
193.	*Semecarpus anacardium* Linn.	Anacardiaceae	Fruits	Rats	Spermatogenic arrest
194.	*Solanum surattense* Burm.f.	Solanaceae	Seed	Rats	Deplete the oxidative stress of cauda epididymal spermatozoa
195.	*Stephania hernandifolia* Willd.	Menispermaceae	Leaf	Rats	Inhibition of spermatogenesis
196.	*Stevia rebaudiana* Bertoni	Asteraceae	Whole plant	Rats	Decrease in Testosterone Level
197.	*Striga orobanchoides* Benth	Scrophulariaceae	Whole Plant	Rats	Antispermatogenic effect
198.	*Syzygium cuminii* Linn. Syn. *Eugenia jambolana* Lam.	Myrtaceae	Oleanolic acid isolated from the flowers of Eugenia jambolana	Rats	Arrest of spermatogenesis
199.	*Tagetes erecta* L.	Asteraceae	leaves	-	Emmenagogue
200.	*Tanacetum parthenium* L.Sch.	Asteraceae	Plant without Root	-	Abortifacient
201.	*Taxus baccata* Linn.	Taxaceae	Leaves	Rats	Antifertility
202.	*Terminalia arjuna* Wight & Arn.	Combretaceae	Bark	-	Antispermatogenic effect
203.	*Tinospora cordifolia* (Willd.) Miers ex Hook.f. Thoms	Menispermaceae	Stem	Rats	Reduction in testosterone levels
204.	*Trichosanthes cucumerina* Linn.	Curcubitaceae	Whole plant	Rats	Antiovulatory activity
205.	*Trigonella foenumgraecum* Linn.	Fabaceae	Seeds	Rabbits	Antifertility activity
206.	*Tripterygium hypoglaucum* (Level) Hutch	Celastraceae	Root Xylem	Humans	Reduced Sperm concentration and motility
207.	*Tripterygium wilfordii* Hook f.	Celastraceae	Root and Isolated plant fractions	Rats and Humans	Reversible infertility
208.	*Tylophora asthmatica* Wight & Arn	Apocynaceae	Leaf and Stem	Rat	Antispermatogenic effect
209.	*Uraria lagopodioides* Desv.	Fabaceae	Whole plant	-	Abortifacient effect
210.	*Urena lobata* Linn.	Malvaceae	Root	Rat	Inhibition of Spermatogenesis and
211.	*Urginea indica* Kunth.	Liliaceae	Bulb	-	Abortifacient effect
212.	*Uritica diocia* Linn.	Urticaceae	-	-	Abortifacient effect
213.	*Urospatha antisylleptica* R.E. Schult.	Araceae	-	-	Contraceptive
214.	*Valeriana Montana Linn.*	Valerianaceae	Root	-	Sterilizer
215.	*Ventilago neo-caledonica Schlecht.*	Rhamnaceae	Leaf	-	Contraceptive
216.	*Vernonia amygdalina Delile*	Asteraceae	Root	-	Antifertility effect
217.	*Viburnum foetidum wall*	Caprifoliaceae	Leaf	-	Emmenagogue
218.	*Vigna unguiculata* (Linn.)Walp (Cowpeas)	Fabaceae	-	Rat	Antifertility effect
219.	*Vitex negundo* L.	Lamiaceae	Seeds	Dog	Anti-Androgenic Effect
220.	*Waltheria Americana Linn*	Sterculaceae	-	-	Abortifacient Effect
221.	*Wedelia gracilis* Rich	Asteraceae	Whole plant	-	Abortifacient Effect
222.	*Wedelia trilobata (L.) Hitch.*	Asteraceae	-	-	Antifertility effect
223.	*Withania coagulans (Stocks.) Dunal*	Solanaceae	Fruit	-	Emmenagogue
224.	*Withania somnifera Dunal*	Solanaceae	Fruit	Rats	Decreased Sperm motility
225.	*Xanthium spinosum Linn.*	Asteraceae	Leaf	-	Contraceptive
226.	*Xylopia aethiopica (Dunal) A.Rich*	Annonaceae	Fruit	Rats	Antifertility effect
227.	*Zaluzania triloba (Ort.) Pers.*	Asteraceae	Plant without root	-	Abortifacient

228.	*Zingiber roseum* (Roxb.) Roscoe	Zinziberaceae	Stem	-	Antifertility
229.	*Zinziber officinale Rosc.*	Zinziberaceae	Rhizome	Rats	Abortifacient
230.	*Ziziphora tenuior Linn*	Labiatae	Seed	-	Emmenagogue
231.	*Ziziphus nummularia (Burm.f.)*	Rhamnaceae	Root bark	-	Abortifacient
232.	*Zizyphus jujuba* Mill.	Rhamnaceae	Bark	-	Antifertility
233.	*Zizyphus xylopyrus (Retz.) Willd.*	Rhamnaceae	Fruit	-	Induces Sterility



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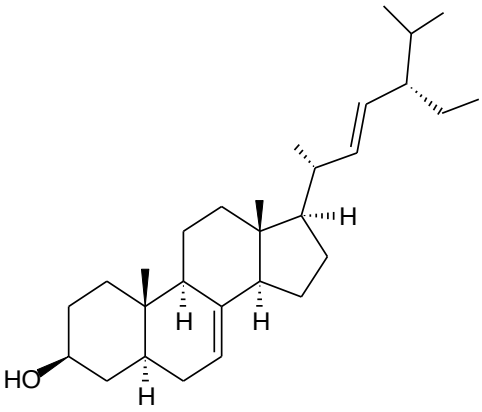

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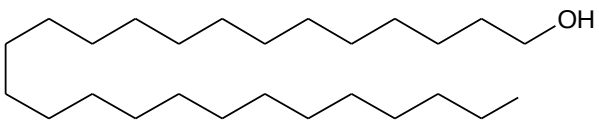

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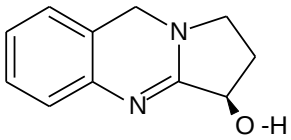

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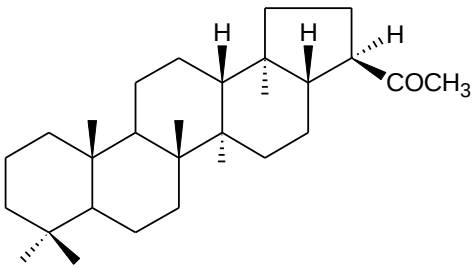

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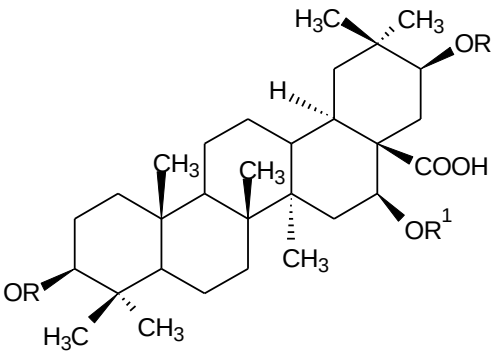

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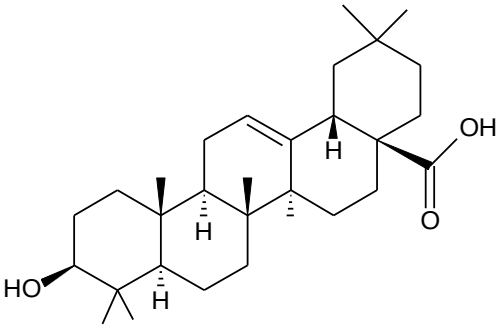

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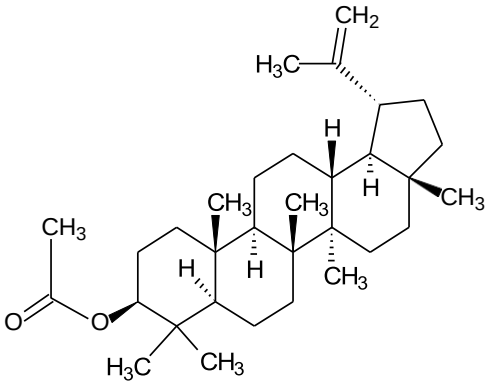

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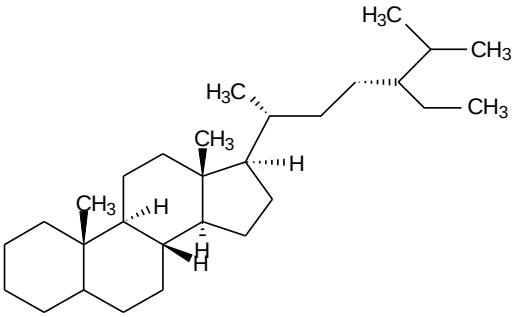

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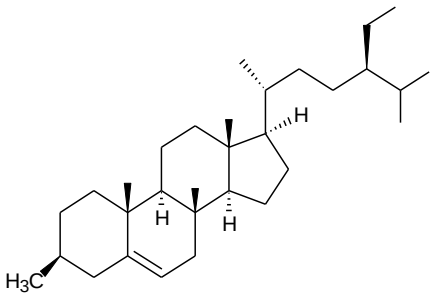

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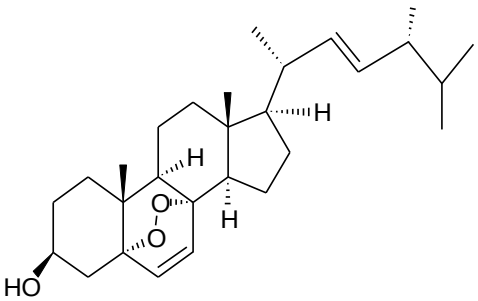

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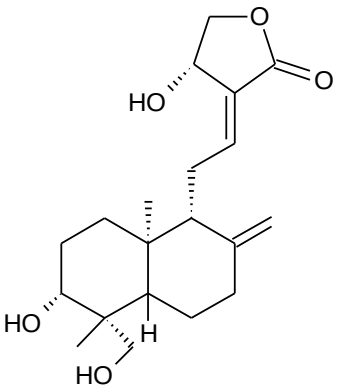

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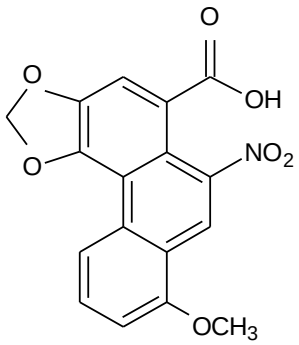

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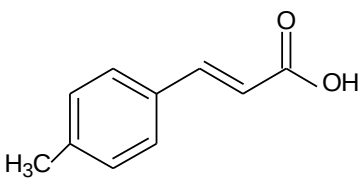

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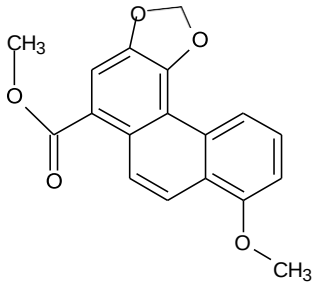

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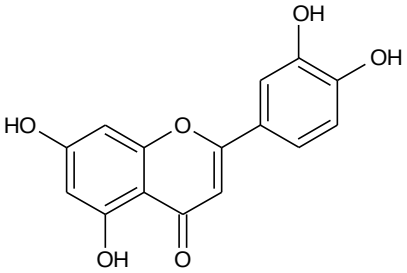

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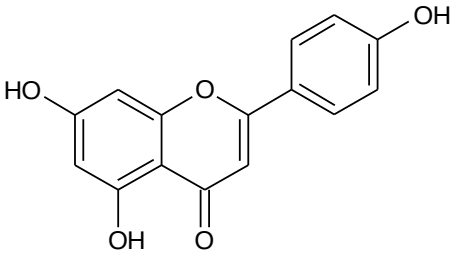

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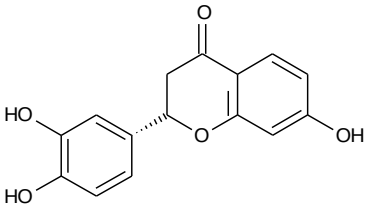

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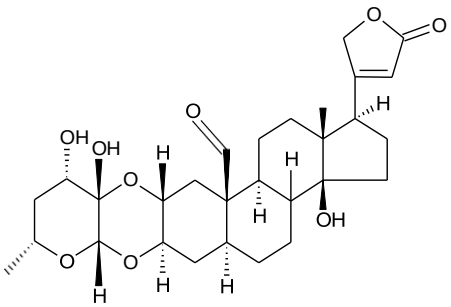

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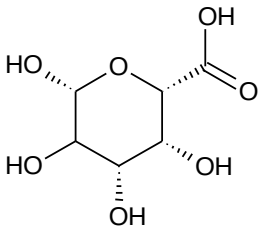

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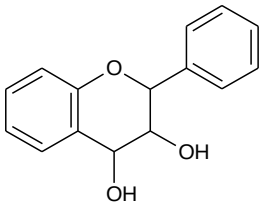

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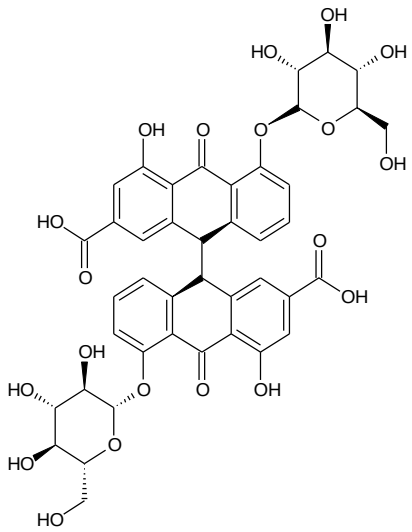

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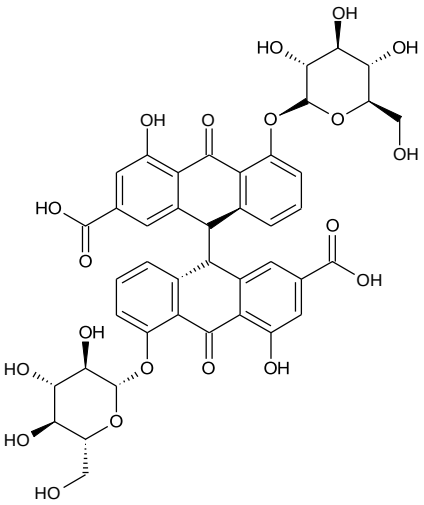

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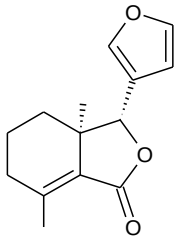

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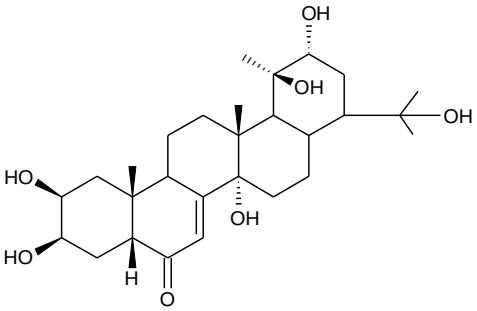

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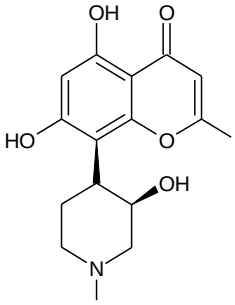

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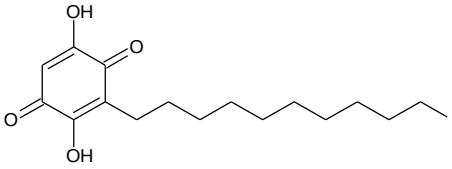

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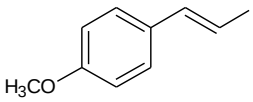

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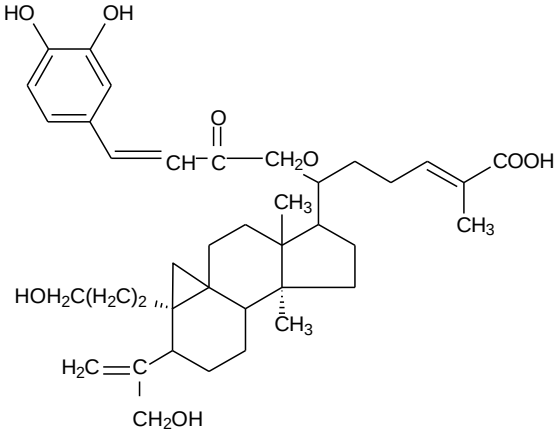
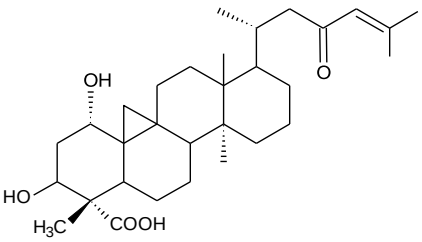


Gardenic acid



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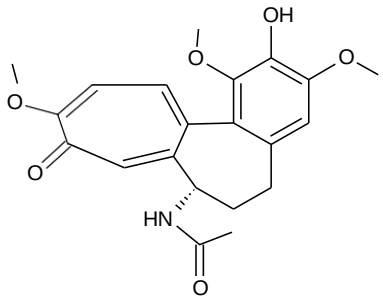

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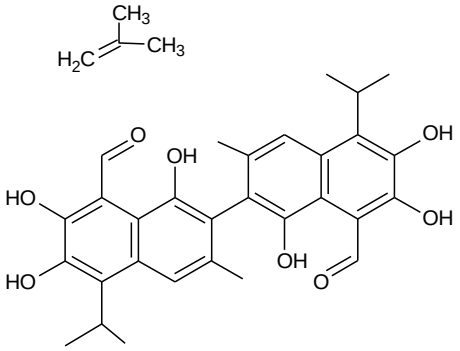
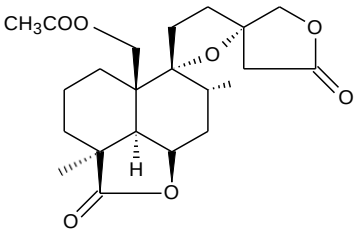


Gossypol acetic acid



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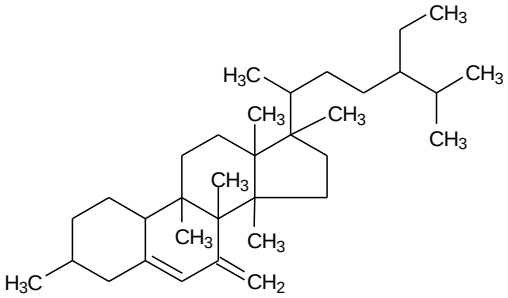
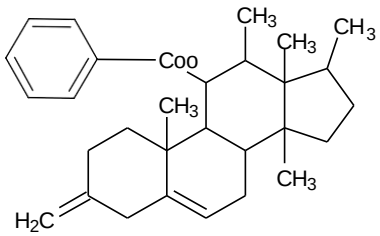


7 -Oxo -beta -sitosterol



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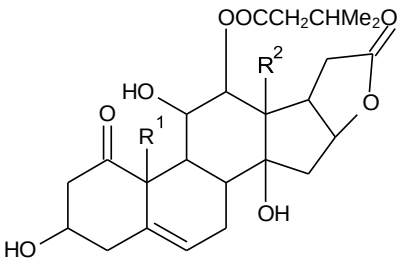

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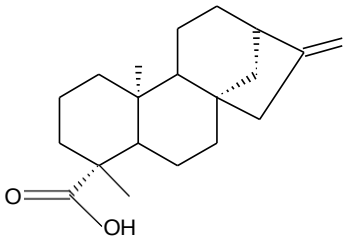

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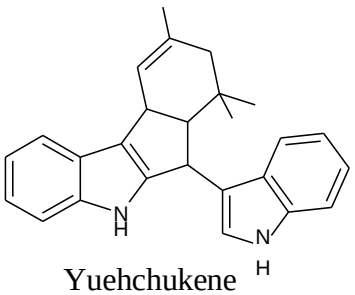

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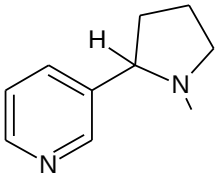

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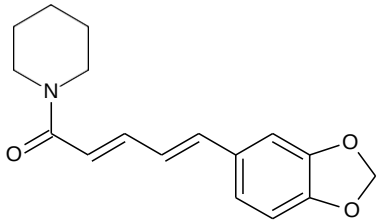

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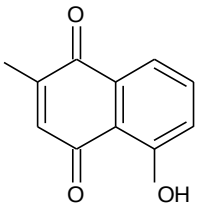

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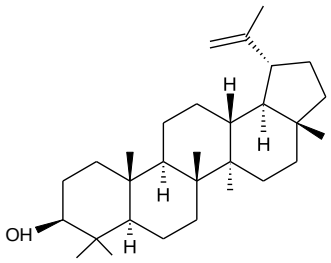

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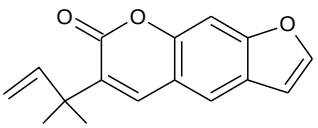

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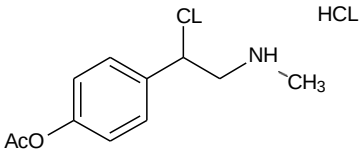

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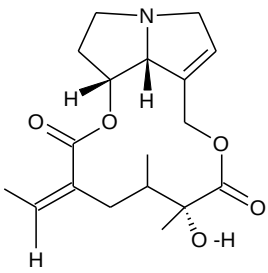
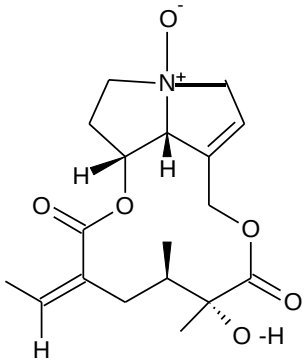
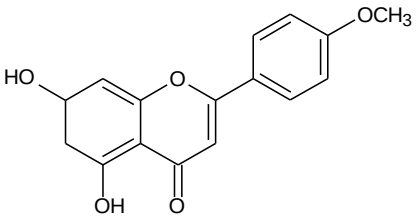


Senecionine



Senecionine N -oxide



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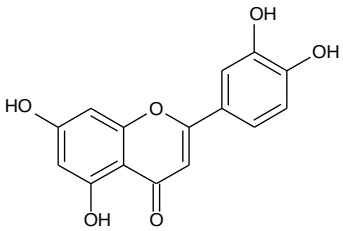

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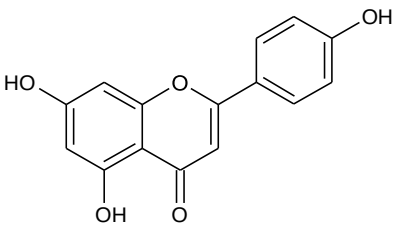

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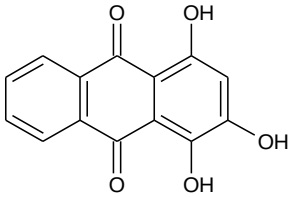

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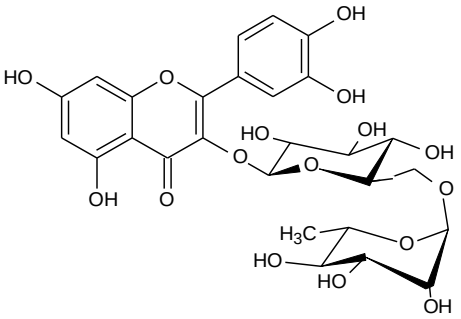

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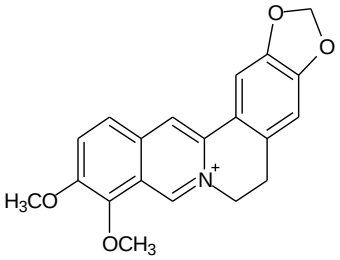
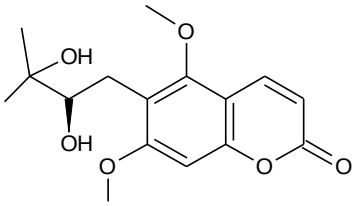


Berberine



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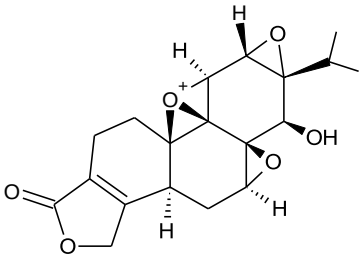

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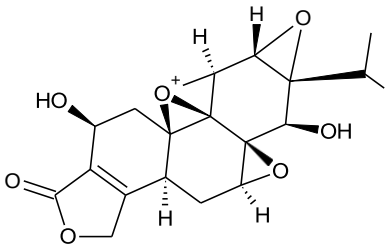

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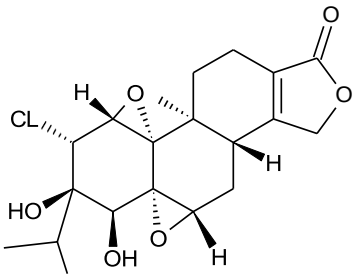

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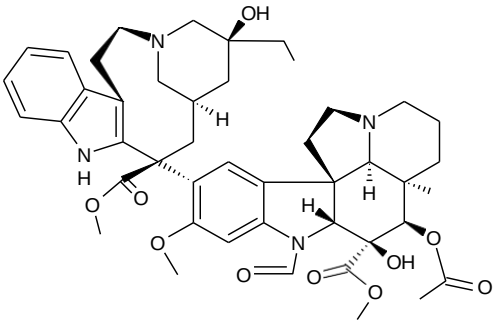
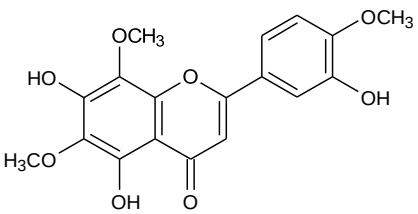
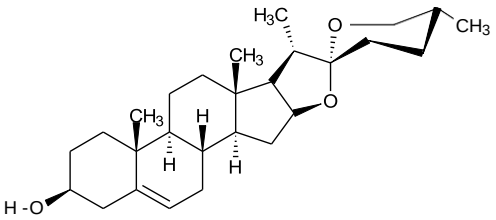


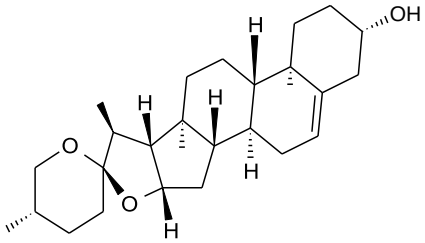
Vincristine



5,7,3' -trihydroxy -6,8,4' -trimethoxy (Acerosin)



Diosgenin



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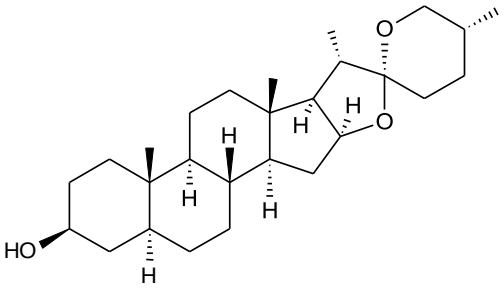

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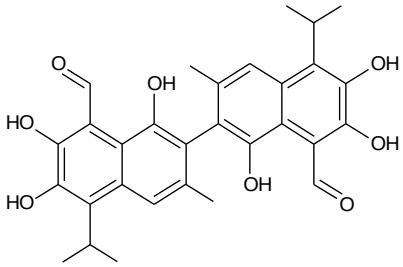

Gossypol

Figure 1: Structure of a Few Chemical Components that Were Isolated from the Plants on the List

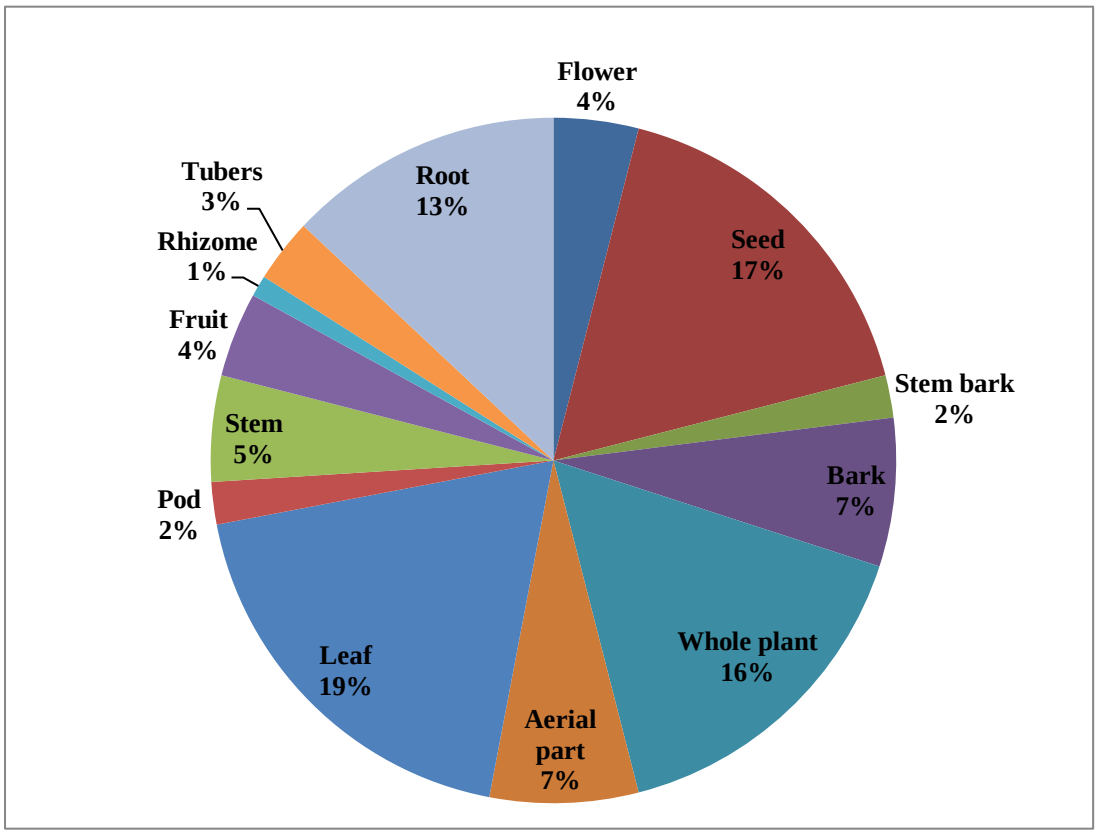

Figure 2: Percentage of Different Plant Parts Responsible for Antifertility Activity

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Entropy and the Lymphatic System, a New Model with Therapeutic Potential

By Philip D. Houck

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Keywords: entropy, lymphatic system, glymphatic function, inflammation, progenitor cells, hs-crp, health model, biological order, regeneration, systems biology.

GJMR-B Classification: NLMC: WH 700

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I. Introduction

Entropy is not a term commonly used in the study of biology. To be more in line with fundamental physical principles, the purpose of this paper is to advance biological concepts to include entropy. Life is seen everywhere on our planet, and we have rudimentary descriptions of life. A definition of life proposed by Macklem and Seely; is

> *"A self-contained, self-regulating, self-organizing, self-reproducing, interconnected, open thermodynamic network of component parts which performs work, existing in a complex regime which combines stability and adaptability in the phase transition between order and chaos, as a plant, animal, fungus, or microbe."* (*1*)

The description between order and chaos is entropy. I personally prefer the mathematical definition by physicist Erwin Schrödinger (1944), "What Is Life? The Physical Aspect of the Living Cell".

> *"How would we express in terms of the statistical theory the marvelous faculty of a living organism, by which it delays the decay into thermodynamically equilibrium (death)? We said before: 'It feeds upon negative entropy', attracting, as it was a stream of negative entropy upon itself, to compensate for the entropy increase it produces by living and thus to maintain itself on a stationary and fairly low entropy level. If D is a measure of disorder, its reciprocal, l/D, can be regarded as a direct measure of order. Since the logarithm of l/D is just minus the logarithm of D, we can write Boltzmann's equation thus:*
>
> *-(entropy) = k log (l/D).*
>
> *Hence the awkward expression 'negative entropy' can be replaced by a better one: entropy, taken with the negative sign, is itself a measure of order. Thus, the device by which an organism maintains itself stationery at a fairly high level of orderliness (= fairly low level of entropy) really consists continually sucking orderliness from its environment".* (*2*)

Statistical entropy described by Boltzmann was used to explain gas molecules in a container and the thermodynamic principle of entropy was used by Carnot to explain the efficiency of steam engines. Negative entropy providing order was introduced by Schrödinger. Further development using energy to provide order has not been advanced. Biology illustrates transient reprieve from chaos. Although chaos is the direction of the universe, transient reprieve from chaos can be seen everywhere with stars being born from star destruction.

Health is maintenance of order The mechanism of maintaining order is the subject of this paper with emphasis on the organ of negative entropy - the lymphatic system. Processes providing negative entropies to maintain order are:

1. Utilize environmental energy to combat chaos (process energy sources - food)
2. Remove metabolic debris (take out the garbage)
3. Adaptation to the environment to maintain homeostasis (dry land requires salt and water management, calories sources changes – protein, fat, carbohydrate)
4. Protection from the environment, invaders, predators, identify self-versus non-self (fight to stay alive)
5. Repair broken parts by aiding stem cells to differentiate and reach their targets (repair battle wounds and replace aging cells) - Electromagnetic information management targets and replaces cells.

Disease is failure to perform the 5 processes listed. Chaos wins the battle when these processes fail, and the organism reaches maximum entropy of room temperature. The lymphatic system performs all the 5 processes and should be considered the organ of negative entropy.

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II. Processes of Negative Entropy with an Evolutionary View

The five processes can be traced with an evolutionary view. When individual cells became a community of cells, life had to obtain energy, remove metabolic byproducts, maintain homeostasis with the environment, protect the colony from foreign invaders, and assure persistence by devoting energy to reproduction (*3 – 5*). Insects evolved early before mammals shortly after moving from water to land habitat. These segmented species were the first to incorporate the immune system with a circulatory system. The system is an open system supplying nutrition to cells, removing metabolic debris, providing protection from environmental threats and hemocytes to repair damaged cells (*6*). The open circulatory system fulfills all the processes required to maintain order.

Segmentation of insects was an advantage decreasing the steps required to evolve into a complex organism (*7*). New species composed of similar segments had an advantage developing slightly different characteristics of individual segments to benefit the organism. In more complex organisms the evolutionary steps would be nearly impossible. Manipulation of genetic code by point mutation directed by environmental advantage is unlikely to result in a complex immune system within current time constraints. The lymphatic system, the segmented evolutionary ancestor of the insect hemolymph is incorporated into nearly all species suggesting the entire system has been shared and refined.

A proposed chimeric evolution incorporating entire systems would speed evolution explaining why so much of the genic code is shared (*8*). Insect hemolymph can still provide valuable insight in the study of the human lymphatic system. Humans likely share a chimeric relationship with arthropods. Considering the proposed evolution from insects, the human lymphatic system likely has segmented properties.

III. Relevance of Lymphatics in Organ Systems to Maintain low Entropy

The human lymphatic system is difficult to visualize limited to swollen limbs. Previously, the existence of lymphatic circulation in organs, blood vessels, and especially the brain was not appreciated. Embryology of the lymphatic system is different from arteries and veins (*9*). Neglecting the role of lymphatics in specific organ systems was a result of information deficit. Magnetic Resonance Imaging (MRI) viewing free water in interstitial space is an indirect measure of lymphatic function. Understanding the role of the lymphatic system in the context of reducing entropy by the 5 processes allows conjecture of their importance in health of organ systems. Enhancing lymphatic functions to lower the entropy of the individual has potential for extending biological age.

a) Gastrointestinal System

All energy enters through the oral cavity from the environment including invaders. The unutilized energy substrate is removed by the cecum. Eating, obtaining nutrients and energy, is the most inflammatory daily process determining the microbiome. The intestinal system has a rich lymphatic network to transport these nutrients and serve as a gatekeeper preventing invaders from harming the collection of cells we call human. The gut hormones have influence on the lymphatic system (10). The lymphatic system, besides transporting nutrients, is the immune system, providing protection from environmental invaders (negative entropy). This function of immunity is also responsible for unchecked inflammation causing disease (positive entropy). Hs-CRP (high sensitivity C-Reactive Protein) is a biomarker reflecting systemic inflammation. An unhealthy microbiome activating unchecked inflammation is measured by the biomarker CRP. CRP is evolutionary conserved and is crucial to immune function (11). CRP exists in two forms, a pentameric and a monomeric form explaining how it can function in both disorder (positive entropy) and influence repair (negative entropy) (12). This biomarker has a mortality prediction. CRP depending on its form can have positive or negative influence on the lymphangion both causing and resolution of interstitial edema and inciting and resolution of inflammation.

Hypertension, a risk factor, can be related to homeostasis of environmental salt and water. The endothelium of lymphatics can store excess sodium (*13*,*14*). If this system fails intravascular volume increases blood pressure. Lymphatics are in blood vessel walls and contribute to lipid deposition, inflammation, repair. Failure of these arterial wall lymphatics will harden the arterial wall increasing pulse wave velocity, a powerful predictor of mortality and systolic hypertension.

Hormones produced by the gut have significant control of lymphangion function. Sodium-Glucose Transport Protein 2 (SGLT2) Inhibitors, glucagon-like peptide 1 (GLP-1) agonists have impacted patient care in means beyond current explanations with the most likely explanation of Lymphangiontrope an enhancement of removal of interstitial fluid and anti-inflammatory effects.

b) Kidney

Homeostasis of fluid and electrolytes, stimulating hematopoiesis, removing metabolic by-products are processes of reducing entropy. The kidney has a network of lymphatics maintaining tissue fluid in an organ responsible for the body's maintenance of this same fluid. Kidney swelling occurs in heart failure when pre-load increases. Kidney swelling also occurs in

inflammatory states. If the lymphatics have dysfunction, kidney swelling will decrease its filtration rate with an increase in creatinine. Chronic kidney disease is associated with albuminuria representing Lymphatic dysfunction.

Sodium-Glucose Transport Protein 2 (SGLT2) Inhibitors help decongest the kidney, reduce albuminuria, and remodel the cardiovascular system (15). The gut hormones glucagon-like peptide 1 (GLP-1) agonists have positive effects on the lymphatic system (16). Both reduce the biomarker Hs-CRP and increase the function of circulating progenitor cells.

c) *Lungs*

The lungs have a rich network of lymphatics due to the lungs being exposed to the environment full of potential invaders. Inflammatory markers of CRP and Procalcitonin are indictors of infection (17). Smoking introduces antigens that further increase inflammation. The chest X-ray remains the most reliable evidence for failure of lymphatics to remove interstitial edema.

d) *Heart*

The heart is central in the closed circulatory system. The lymphatics of cardiac structure are poorly studied. The pathological condition of Tako Tsubo syndrome suggests the segmented disease presentation is consistent with the segmented distribution of lymphatics. The proposed mechanism is a regional reduction in the Lymphangion function with tissue accumulation of fluid. After recovery of lymphangion function the tissue edema is removed restoring cardiac function to normal. Pathophysiology remains elusive (18). The heart has metabolic demands with associated increased entropy. Lymphatics are crucial to combating chaos. The heart produces natriuretic peptides that are the most effective stimulus to lymphangion function. The heart signals peripheral lymphangion to compensate for a failure of the closed circulation by increasing the function of the open circulation.

The ultimate therapy for cardiac dysfunction is injectable Brain Natriuretic Peptide (BNP) with a neprilysin inhibitor. In fact, this therapy would aid any disease process of impaired lymphatic function due to lymphangiontrope of BNP. BNP increases the frequency and amplitude of the lymphangion (19). Injectable BNP with a neprilysin inhibitor is not a current therapy. Angiotensin receptor blocker with a neprilysin inhibitor is an approved therapy but relies on the patients intrinsic BNP. If the intrinsic BNP is not a *functional therapy (BNP resistance) the therapy may fail.*

e) *Blood Vessels*

Endothelium, the lining of blood vessels has the greatest representation of cell type in the human body. Risk factors reduce the number of circulating endothelial progenitor cells. Lymphatics are also composed of endothelial cells and supply a rich network to the blood vessels as noted above in hypertensive subsection. The system helps repair endothelium by transporting progenitor cells and removing senescent cells. Lymphatics also transport lipids and inflammatory cells. Atherosclerotic progression and regression are governed by this system under the influence of environmental diet and inflammation. Health is maintenance of good endothelial function supplied by the organ of negative entropy the Lymphatic system.

f) *Brain*

High metabolic activity supported by high blood flow and increased oxygen extraction make the brain a highly entropic organ. The amount of negative entropy used to maintain a memory over many years is high and maintenance of memory is poorly understood. Some of the systems which help maintain low entropy are the blood brain barrier to limit foreign invaders, a rinsing supply of cerebral spinal fluid and a glymphatic system to remove the metabolic products (20). Sleep is necessary to enhance lymphatic function. During sleep the brain shrinks in size, increasing glymphatic flow and cerebral spinal flow. Sleep allows reordering of brain function (21). The glymphatic also helps repair cellular senescence by progenitor transport. The Lymphatics role in brain diseases was discussed in a paper Lymphatics: Future Perspectives Unrealized Potential (22). Those concepts are repeated with an entropic view and further propose novel therapies for brain diseases including schizophrenia, depression, anxiety, and Down's Syndrome. All these conditions have biomarker evidence of increased inflammation and therefore reduced glymphatic function (23-29).

i. *Down's Syndrome*

Down's syndrome trisomy 23 is a congenital condition. The chromosomal addition, 47 total, increases the entropy of these patients resulting in shortened life spans. In addition to chromosomal entropy these patients are born with increased inflammation as evidenced by elevated Hs-CRP, increased at birth remaining elevated throughout lifespan and contribute to early mortality. The higher the biomarker of Hs-CRP the greater the intellectual deficits (30). Inflammation increases the entropy of the brain by reduced glymphatic removal of waste products. Down's Syndrome represents glymphatic dysfunction of the brain inhibited by CRP with failure to eliminate byproducts of brain metabolism increasing the entropy of the brain. Schizophrenia, depression, anxiety, also have an elevated biomarker of CRP and again the mechanism of brain dysfunction is proposed as glymphatic dysfunction. If therapy can be administered that reduces inflammation and reduces the biomarker Hs-CRP, glymphatic function will improve with preservation of learning, intelligence, and improvement

of well-being. There are ethical concerns treating infants with their inability to give consent. The therapies for infants will need to be low risk therapies to justify their use to prove this hypothesis. Therapies for mental illness in adults can be more easily tested with therapies known to reduce CRP.

ii. *Brain Remodeling versus Neurotransmitter Theory*

Until recently, the glymphatic system was not recognized. Over the last 120 years receptors and proteins known as neurotransmitters have been discovered (*31*). This knowledge ushered in pharmacological therapies for brain diseases. The disconnect in the therapeutic response of the neurotransmitter theory is the time frame needed for recovery, estimated to be 6 to 8 weeks. If it was truly a deficit of neurotransmitters the ailment would only take hours to correct. Improvement over 6 to 8 weeks suggest remodeling of brain structure is required. Serotonin, Dopamine, Histamine increase the amplitude and frequency of the Lymphangion (*19*,*32*). The suspected benefit of these neurotransmitter drugs is the negative entropy provided by improvement of glymphatic function and brain remodeling.

g) Biomarkers of Lymphatic Failure

Failure to maintain order in any of the organ systems will result in increasing entropies with a reduction in lifespan. Table 1 summarizes organ systems dysfunction due to lymphatic failure by risk factors and biomarkers. Albuminuria, Hypertension, elevating creatinine, infiltrates on chest x-ray, rising Brain Natriuretic Hormone BNP, reflect failure to manage interstitial fluid. Hs-CRP, Cystatin C, Procalcitonin reflect aberration in the inflammatory system. Circulating progenitor cells, troponin are markers of repair and destruction respectively. The lymphangion is a source of troponin in addition to the heart (33,34). The source of troponin in serious medical conditions is likely from the lymphangion and not the heart. The lymphatic system functions in taking out the garbage, managing inflammation and repair fulfilling the 5 processes. Elevated troponin representing dysfunction of the organ of negative entropy has dire outcomes.

Table 1: Organ Biomarkers/Risk Factors of Lymphatic Dysfunction

Organ	Biomarker/Risk Factor
Gastrointestinal	Hs-CRP Hypertension
Kidney	Albuminuria Creatinine Cystatin C
Lungs	Chest X-Ray CRP Procalcitonin
Heart	Natriuretic peptides Troponin
Blood Vessels	Circulating Progenitor cells
Brain	Hs-CRP

IV. Negative Entropy - A Shift to Biological Repair –Therapeutic Options Proposed

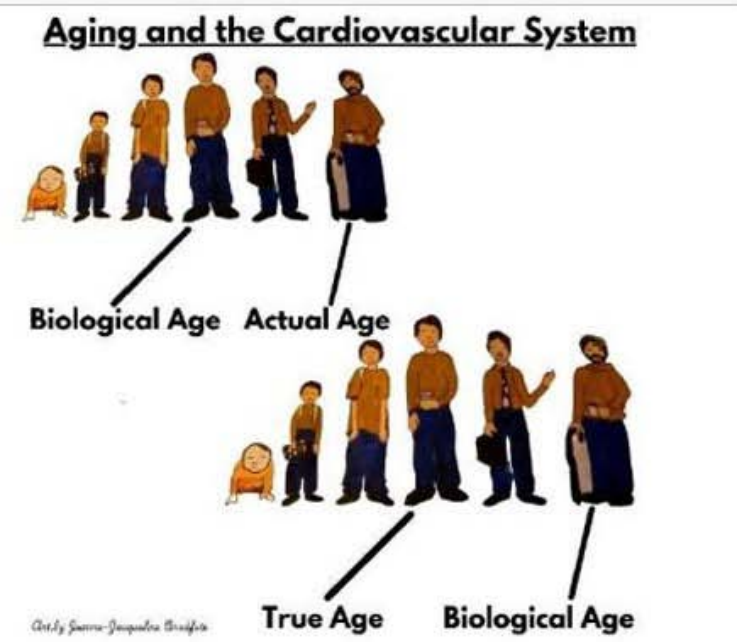
A shift in biological therapeutics toward modification of inflammation is actively under development after a very slow beginning. An additional shift to repair mechanisms in biology is still only a glimmer of hope. Both therapeutics are necessary to prolong disease free aging. Repairing organs and the entire organism is necessary to maintain a low entropic state. It is estimated the cell turnover rate is 330 billion cells per day (*35*). Failure of repair will increase entropy and shorten lifespan. Currently, therapies to enhance repair are nonexistent. Negative entropy requires both repair of senile and damaged cells and controlling inflammation; responsible for removing those cells and paradoxically killing cells under other circumstances. Again, the lymphatic system's role in both processes emphasize the statement lymphatics are the organ of negative entropy.

Positive lymphangiontrope is an invented term defined as an increase in the amplitude and frequency of the lymphangion secondary to an intervention. The intervention may be pharmacological, mechanical or electromagnetic. Pharmacologic study in animals has been in mesenteric vessels and is summarized by Russel (*32*). There is also some confusion in these interventions since there seems to be occasional opposite responses of the lymphangion and the conductance ducts. The lymphangion is a work horse operating at the tissue level. The ducts tone will affect diastolic flow and is sensitive to the preload of the closed circulatory system. Examination of therapeutic options will be limited to increasing lymphangion function and ignoring the effect on conductance vessels. Lymphangiontrope should also be measured by the efficiency of directing progenitor cells and management of inflammatory responses.

Positive lymphangiontrope, negative entropy, can be inferred from studies in rat mesenteric vessels

with visual measures of lymphangion amplitude and frequency and transport of cells. Older rats have a reduction in lymphangiontrope (*36*), suggesting the increasing entropy of aging is due to decreasing lymphangiontrope. Activation of T cells, B Cells, cytokines, and antibody management are an additional function of the lymphatic system. The sum of these processes is very complex. The results of these processes can be integrated into mortality outcomes. Clinical trials with a reduction in mortality represent the process of negative entropy implying a favorable impact by lymphatics role in inflammation and repair.

All the moving parts of the lymphatic system are difficult to study but can be seen as lifespan. In disease states clinical trials demonstrate a mortality benefit increasing lifespan. Studies with interventions in healthy adults for the purpose of extending life are few. Risk factors in a healthy population predicting future disease states reducing lifespan have been studied. Biologic age is reduced by risk factors, poor lifestyle, adverse biomarkers of inflammation and repair (*37*). Figure 1 used with permission shows the odds ratios ranked in order of importance of relative all-cause mortality. The lower the ratio, the shorter the lifespan, the greater the positive entropy of the biomarker. The odds ratios from their sources had appropriate confidence intervals and were statistically significant. A reduction in biological age reflects increasing entropy. Medications and interventions moderating risk factors have mortality benefit suggesting the intervention had negative entropy.



Contributors to Increased Biologic Age

Years of Life Lost to Modifiable Risk

Order of Importance

Bio Marker / Risk Factor	Odds Ratio All-Cause Mortality
Pulse Wave Velocity	.16
Glucose Intolerance	.3
Six-Minute Walk distance	>414 to <290 1.0 to .37
Smoking	.47
Hypertension	.57
Circulating Stem Cells	.61
Waist Circumference	.60 –men .64 - women
ECG Findings RAE LAE LVH	 .67 .63 .53
Hs-CRP ≥ 2.0	.7
Frailty	.84 – men .88 - women
Number of Co-Morbidities	.89 – men 1.0 - women
Coronary Artery Calcium >400	.9
Short Sleep <7	.9
Cholesterol	.9

Fig. 1: Contributions to Biologic Age with permision Houck P. The Era of Risk Factors Should End; the Era of Biologic Age Should Begin. *Hearts*. 2025; 6(1):2. https://doi.org/10.3390/hearts6010002 The lower the odds ratio the greater the impact of entropy due to biomarkers and comorbidities

V. Model of Health and Disease

Inflammation and repair are represented by Hs-CRP and circulating progenitor cells. The biomarkers of elevated Hs-CRP and reduced circulating progenitor cells have an odd ratio of .7 and .61 respectively from Figure 1. Both biomarkers are also dependent on risk factors. Both biomarkers reflect inflammation and repair and are a predictor of reduction in lifespan. The other biomarkers of a reduced lifespan are seen in Figure 1. can also be related to inflammation and failure to repair or remodel. Smoking, hypertension, metabolic syndrome of diabetes, and waist circumference is linked to stress on the lymphatic system.

A model of health and disease was previously presented (*38*). This model considers health when regeneration and degeneration are balanced by the moving fulcrum controlled by inflammation. The model demonstrates the importance of the immune system in both proliferative diseases such as cancer and degenerative diseases such as age and mental illness. Diabetes I is a degenerative disease due to insulin deficit, whereas Diabetes II is aproliferative disease due to insulin excess. The fulcrum is controlled by lymphatic function. Lymphatics also participates in circulating progenitor cells. Figure 2 is a further refined model emphasizing positive and negative entropy with interventions that modify progenitor cells and inflammation in both positive and negative manners. Medication intervention reducing all-cause mortality by modifying Hs-CRP and circulating progenitor cells is seen in Table 2. The odds ratios from the reference have appropriate confidence intervals and were statistically significant. Some of the interventions are listed under both circulating stem cells and a reduction in Hs-CRP and are noted by *italics*.

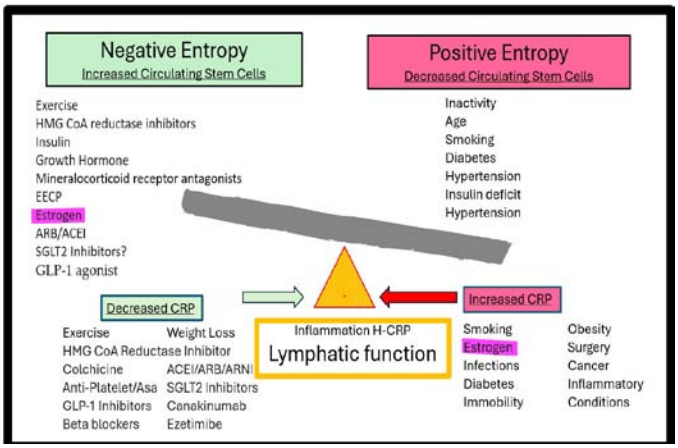


Fig. 2: Model of Health and Disease Balancing Positive and Negative Entropy by Lymphatic Function

Table 2: Odds Ratio of All-Cause Mortality of Medications Modifying Inflammation (Hs-CRP) and Repair (Circulating Progenitor Cells)

Inflammation/Repair Biomarkers	Modifying Medications Interventions	Absolute Mortality Odds Ratio	Reference
Circulating *Progenitor* Cells	*Exercise*	.68	(*39*)
	HMG CoA reductase inhibitors	.86	(*40*)
	Mineralocorticoid receptor antagonists	.82	(*41*)
	Estrogen under 60	.61	(*42*)
	over 60	1.03	(*42*)
	ARB/ACEI	.98	(*43*)
	SGLT2 Inhibitors?	.75	(*44*)
	GLP-1 Agonist	.88	(*45*)
Hs-CRP Continued below	*Exercise*	.68	(*39*)
	Weight Loss	.85	(*46*)
	Statin	.86	(*40*)
	Colchicine	1	(*47*)
	ACEI/ARB	.98	(*43*)
	ARNI	.66	(*48*)
	SGLT2 Inhibitors	.75	(*44*)
	GLP-1 Agonist	.88	(*45*)
	Mineralocorticoid receptor antagonists	.82	(*41*)
	Canakinumab	.66	(*49*)
	Ezetimibe post MI	.77	(*50*)

VI. Discussion

Messages from Figure 1, 2, and Table 2 reveal lack of exercise will decrease circulating stem cells and increase the inflammatory state. As the distance of six-minute walk decreases, frailty increases, obesity and metabolic syndrome become further manifestations increasing Hs-CRP. The lack of exercise as measured by the six-minute walk is a powerful predictor of short-term survival. From Table 2. The odds ratio of total absolute mortality for exercise is .68, the best of all the interventions. Exercise is clearly needed for enhancing lifespan and improving lymphatic function. Diseases of the brain a failure of glymphatic function should be treated with exercise as a primary modality.

HMG CoA Reductase Inhibitors, Mineralocorticoid receptor antagonists, SGLT2 Inhibitors, GLP-1 Agonist, also are listed as agents that reduce Hs-CRP and increase circulating stem cells with improvement of lifespan. These agents are favorable to the lymphatic system and should be considered in brain diseases and other diseases of reduced repair and inflammation regardless of a medical condition warranting their use. This statement is bold reflecting achange of direction in medical therapeutics from observation, trial and error to utilization of predictive models to repair a malfunction.The use of these medications is to treat the organ of negative entropy - the lymphatic system to maintain good health.

Estrogen, highlighted by red outline in figure 2 is confusing, having properties of both positive and negative entropy increasing progenitor cells and increasing Hs-CRP making it vascular friendly and prothrombotic proinflammatory. Clinical trials failed to elucidate a female advantage due to the use of fixed dose estrogen. For the purposes of reproduction, immunity is shifted during changes in cyclic estrogen. The shift is necessary to immunosuppress the mother to accept the father's antigens. T helper cell 1 (Th1) is shifted to T helper cell 2 (Th2) altering the Th1/Th2 balance (*51*). This shift favors vascular repair explaining the paradox. Previous clinical trials in estrogen failed to elucidate the female advantage due to fixed dose estrogen. It is time to reinvestigate the female advantage using variable dose estrogen in the perimenopausal period measuring Hs-CRP and circulating progenitor cells in addition to clinical measures.

a) Negative Entropy

Entropy is the second law of thermodynamics – if the system is irreversible the entropy of the system and the environment increases. Statistical entropy described by Boltzmann is a refinement but is limited due to the complexity of systems. The mathematical description represents disorder in all possible states. It can be used to predict gas laws. Debate over the concept of negative entropy raged during the time of Schrödinger and continues. Negative entropy represents the energy of a system to maintain or become more orderly. Two cells becoming one requires energy (negative entropy) and can be calculated. After performing a step in a biological system, the next step may have multiple possible outcomes. If the next pathway is critical there will be carrier protein or energy source directing to a successful outcome representing negative entropy (*52*, *53*). The entropy of a human considers all the parts and how the parts can be arranged. The number of parts is the primary driver of entropy. The virome and microbiome, far out way the number of cells in the human body. These tiny inhabitants of the human body by numbers can cause chaos. The evidence is in pandemics. The study of the virome and microbiome should have priority due to their ability to increase entropy. Systems to reduce entropy are necessary to maintain order and extend lifespan.

Entropy can be a positive force seen in favorable mutations selecting environmental winners – evolution or can be devastating causing disease and fatal consequences. Entropy can misfold proteins, produce aberrant proteins with disease caused by resistance. Drug discovery can be more efficient considering statistical entropy. Improving the organ of negative entropy can extend lifespan.

b) Desired Outcomes Generated by Entropy and the Lymphatic System

B.1: Appreciate lifespan is determined by negative entropy provided by the lymphatic system.

B.2: The brain is a highly entropic organ maintaining order with the glymphatic system.

B.3: Brain diseases should be treated by enhancing lymphatic function, especially exercise.

B.4: Down's Syndrome has a biomarker of therapy Hs-CRP. Interventions during infancy and perhaps prenatal reducing Hs-CRP should be explored – consider BNP.

B.5: Drug development should routinely study lymphangiontrope in rat mesenteric vessels, measure drug affect by Hs-CRP and their effect on circulating progenitor cells.

B.6: Women's health advantage should study variable dose estrogen.

B.7: A simple model of health and disease described as progenitor cells balanced by the lymphatic system can describe complex biology and offer solutions that are obscured by complexity. A simple program can result in complex behavior (*54*).

B.8: Injectable BNP with a neprilysin inhibitor should be studied for lymphatic dysfunction, heart failure, and especially brain diseases including Down's syndrome.

B.9: The relationship of the virome and microbiome to Hs-CRP and circulating progenitor cells should be studied.

VII. Conclusion

Entropy, a fundamental concept in physics and chemistry, is not utilized in the study of biology. Biology must obey the rules of entropy and for a period can maintain order. The method of maintaining order can be modeled by circulating progenitor cells and inflammation controlled by Hs-CRP. The lymphatic system supplies thisorder. Pleiotropic properties of medications can be ascribed to lymphatic function of negative entropy. Interventions providing negative entropies with longer lifespans, include exercise, HMG CoA Reductase Inhibitors, Mineralocorticoid receptor antagonists, SGLT2 Inhibitors, GLP-1 Agonist. In the future, search for therapeutic options should include measurement of lymphangiontrope, Hs-CRP, and circulating progenitor cells.

Future Directions

This paper presents simple rules and a simple model to explain health and disease. These concepts can be accelerated by proving the model. After appropriate validation of the model, it can be used in many scenarios to treat diseases that have no current recommendations. An initial plan of study would be to include measurement of progenitor cells, Hs-CRP

inflammatory changes, and animal models to detect changes of lymphangiontrope by intervention. Understanding the model will lead to repair therapies which will decrease entropy and extend lifespan.

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Effect of Ozoniotherapy in the Treatment of Necrosis after Hair Transplantation: Case Report

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Abstract- *Introduction:* Nowadays, ozone plays an important role in wound healing and tissue repair as a therapy and as antimicrobial, bactericidal and fungicidal agent. It attains recognition in hair transplantation as a treatment for necrosis due to hypoxic-ischemic local syndrome. *Objective:* to demonstrate the therapeutic evolution of ischemia in a hair transplant after ozone therapy sessions. *Methods:* The patient was evaluation and gave consent to photographic records. He went through 30 topic applications of ozonated oil, with a 10 drop dosage daily; 12 bag ozone sessions for 10 minutes; besides subcutaneous applications, with 30% ozone concentration and a very small gas volume (1-2 ml) with 30G needle. *Results:* Evolution of the case was registered with images and tissue coloring and changes evidenced. *Conclusion:* It is clear that ozone therapy made wound healing and tissue repair faster, since there was an increase of epithelial cells and neoangiogenesis due to therapy, resulting in almost complete repair of the patient's hair transplant at the end of the sessions.

Keywords: *ozone therapy, hair transplant, hair treatment.*

GJMR-B Classification: *LCC: RL87.3*

Strictly as per the compliance and regulations of:

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I. Introduction

Hair transplant has been changing many individuals' reality that face alopecia, a disease consisting of head or body hair loss. Unlike several other transplants, hair transplant is in the spotlight because of its peculiarity in using follicles of the same donor who is supposed to receive them in a less invasive way. In spite of the many techniques available, all of them require patient evaluation including: patient history, age, previous medical evaluations. Diagnosing the type of alopecia is mandatory. Whenever the patient has the conditions for the procedure, it is unusual the occurrence of resulting complications. However, as highlighted by Zito and Raggio in Statpearls, "Potential complications include: edema (5%), bleeding (0.5%), folliculitis, infection (less than 1% of patients)". Being the necrosis of the receiving area due to excess density in the area or another possible cause present.

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Hypoxic-ischemic local syndrome, which can evolve to tissue necrosis, develops from low blood perfusion in tissues and decrease in oxygen because of several etiologies, such as abuse of anesthetics and vasoconstrictors and excess of FUs in an area. The appropriate level of oxygen in tissues is fundamental so that cells keep their aerobic metabolism and vital functions. When the perfusion pressure is not enough to keep the minimal oxygen level, aerobic metabolism shifts to anaerobic with resulting organic dysfunctions. Therefore, treatment is an issue of diagnosing the primary cause and should be initiated at the ischemic lesion spot so as to start revacularization.

Necrosis takes place whenever a cell is exposed to extreme environmental conditions, adverse and excessive stimuli, or in face of deleterious mutations codified in its genetic material. Cell necrotic death occurs as a response to severe physiological conditions, including hypoxia, ischemia, toxin exposition, anesthetics, reactive metabolites of oxygen and nutrient deprivation. In cases of ischemic necrosis, nuclear alterations of cytoplasms portray a clotted blood appearance: acidophilus, granular and hardened. There is loss of tissue structure and the area becomes whitish, bulged and hyperemic. Among microscopic aspects there is increase in acidophilus, a granular appearance and formation of amorphous masses as a result of membrane rupture and mixture of autolyzed material.

Ozone therapy, considered an alternative therapy, with excellent results and ease of application, is in evidence in many countries. It was first acknowledged in 1839, by german chemist Christina Friedrich, and in 1896, by Nikola Tesla, who patented the first ozone generator, in the US, used during the First World War to treat gas gangrene, which treatment is still in use.

Ozone therapy is a bio-oxidative therapy based on a gasified mixture of oxygen and medical ozone, whose therapeutic effects include mainly the improvement of metabolism and the oxygenation of peripheral tissues, as a consequence of increased erythrocyte flexibility, allowing for a better flow inside capillaries and assuring a larger supply of oxygen in the tissues. This process facilitates epithelial repair and growth and inhibits bacterial and fungicidal development.

In hair transplantation, despite technological advancements, ozone therapy application to treat ischemic necrosis is unknown or barely known, as

shown by the reduced number of research papers and therapeutic approaches which might be a guidance for professionals in the field. Thus, the current study aimed at making the causes and effects of ozone therapy more clear whenever it is aptly applied to treat and prevent ischemia and necrosis in hair transplantation procedures.

II. Materials and Methods

This is a longitudinal descriptive and interventionist study with convenience, consecutive, non-probabilistic sampling. The patient underwent a hair transplant procedure in May, 2022, in an unknown doctor's office and was referred to Dr. Anayene Craveiro, at Belcorp Institute, after first signs of ischemic necrosis.

The recommendations of the Madrid Declaration on Ozone Therapy were considered to evaluate the appropriate doses for the corresponding mechanism of action. First, there are three basic principles: (1) not to do harm; (2) stagger the dose; (3) apply the necessary concentration.

Treatment was started with initial evaluation and recognition of the ischemic necrotic area, with mediated intervention. Lesion characteristics were evaluated on the grounds of photographic records facilitating the patient's therapeutic evolution follow-up.

The Oxy device, manufactured by Tonederm®, licensed by the Brazilian Health Regulatory Agency (ANVISA), was employed in the treatment. This device turns medical oxygen into ozone gas through corona discharge. Topical treatment with gas, and a plastic transparent bag manufactured with ozone resistant material, consists of applying an elastic band with sealed edges to the skin.

III. Case Outline

A 40-year-old white male patient, with no pre-existing diseases, underwent the hair transplantation procedure in May, 3rd 2022, with 4,600 follicle units.

The patient - himself a doctor - was referred to Dr. Craveiro Mendes in the same week following his noticing of an ischemic area. His exams showed no other symptoms, nor were there any complaints of allergic reactions. On inspection, the lesion showed well defined edges adherent to wound bed with small fibrin clots, wound bed with granular tissue, adjacent skin edema, peeling skin around the tissue lesion and absence of exudate and odor.

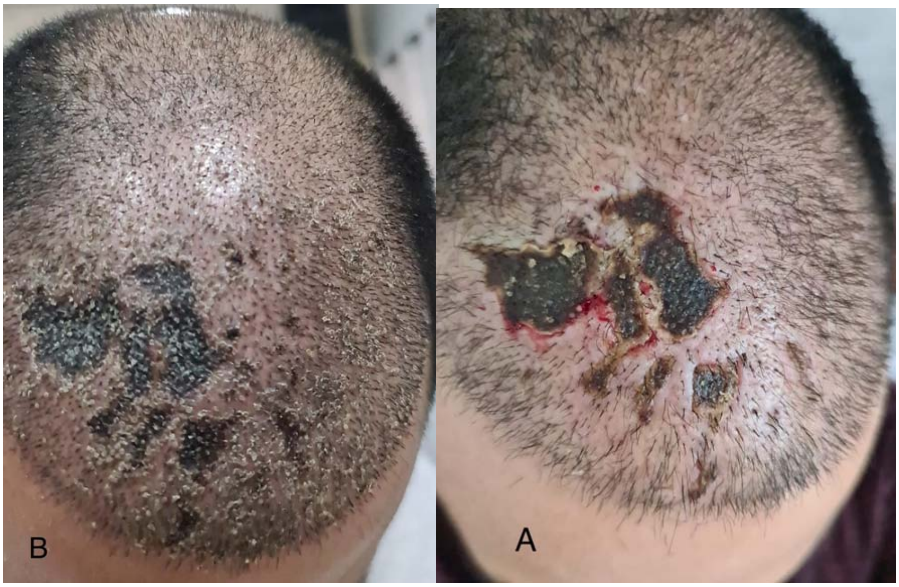
The patient was submitted to 30 ozonized oil topical applications, 10 drops a day, and twelve 30 % ozone sessions with a bag, once a week, for 10 minutes, besides subcutaneous 30% concentration ozone applications with a small gas volume (1-2 ml) through 30G needle. Ozone therapy was conducted after local hygienization with no dressing following the application.

The patient, who unexpectedly faced complications after pursuing hair transplant for high self-esteem, was also provided with psychological care for better acceptance of ozone therapy results.

IV. Results and Discussion

Photographic images demonstrate the progress between the first and last ozone therapy applications. There was local neovascularization and wound healing with progressive reduction of the necrotic area. It is possible to observe at first hand the increased blood supply, vessel permeability and vasodilation, which showed a better coloring appearance since the first session. Granular tissue was found in the first session with endothelial and fibroblast proliferation, which are mesenchymal differentiated cells spreading on the lesion surface. On the first days, angiogenesis first stages were observed with a bulged and whitish region surrounded by a red halo. On the last day it was possible to see a better wound bed and epithelial tissue growth, that is, new skin growing out of the lesion edges in face of a concentration process of the marginal wound walls, under the action of activated fibroblasts, making epithelization possible. It exhibits a shiny rose coloring related to mature collagen.

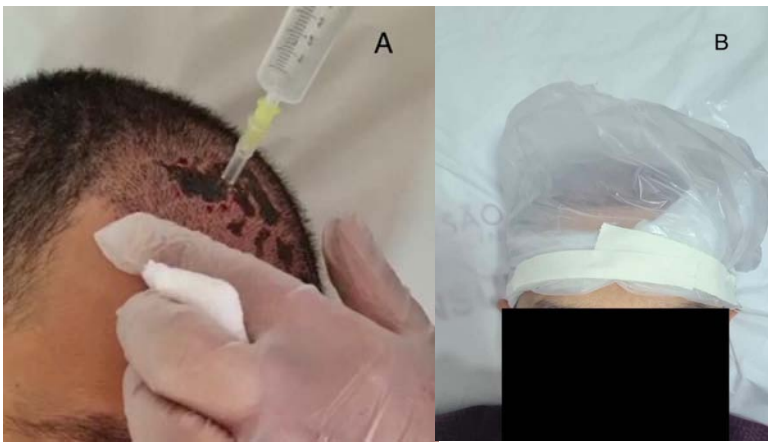
According to the photographic records before and after the three sessions (Picture 1), there was improvement of tissue healing, decreasing bulging, better local blood supply, and recovery of the whitish appearance. In addition, there was growth of granular tissue due to collagen activity, elastin and reticular fibers in an attempt to tissue repair. This phase produces the increase of inflammatory cells, growth factors, vasodilation and presence of permeability.



Source: Author

Picture 1: Before (B) and after (A) of Ozone Therapy Application

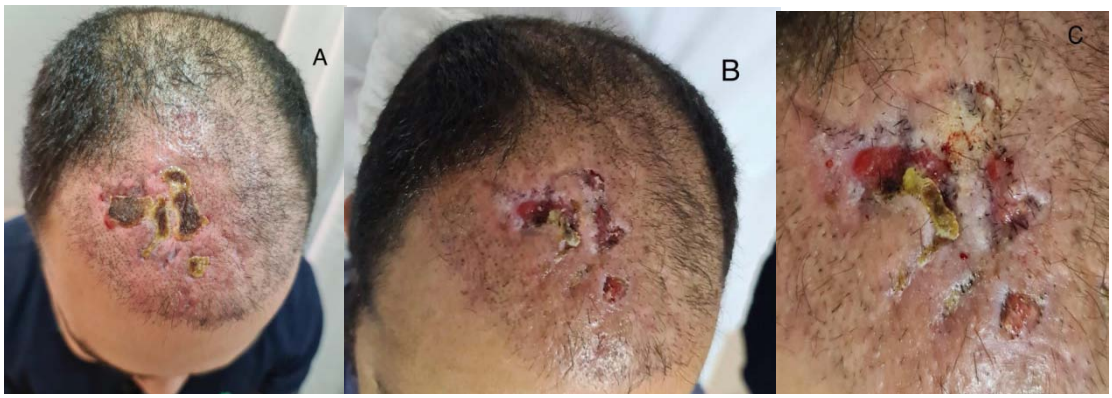
Along the application sessions, there was significant improvement (Picture 2). Necrotic tissue started debriding and granular tissue formation took place, with faster neovascularization and local epithelialization. Studies have demonstrated that ozone oil can promote wound healing through PI3K/Akt/mTOR signaling. Mechanically, it is possible to verify that ozone oil can activate fibroblasts and promote their migration. Besides that it can extend the mesenchymal epithelial transition (MET) process.



Source: Author

Picture 2: Application of Subcutaneous Ozone (A) and Bag Therapy (B)

The analysis of therapeutic evolution after 5 sessions of ozone therapy (Picture 3) makes clear the expansion of mesenchymal cells, fibroblasts, on the wound surface, which is related to internal vessel growth and formation of conjunctive tissue. From this moment, concentration of lesion edges takes place, facilitating epithelization.



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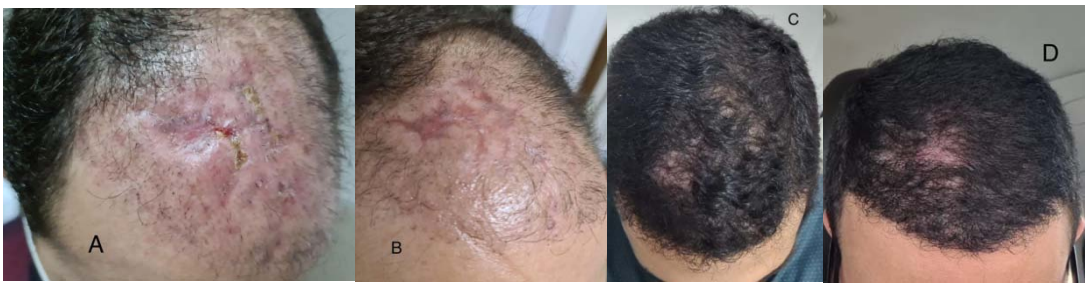
Picture 3: Evidence of mesenchymal cell growth surrounding de lesion (A); Concetration of edges for epithelization in (B) and (C)

Gradually after concluding ozone therapy sessions, remodeling phase starts (Picture 4) leading to reduction of cell activity and blood vessels, Then, maturation and increased local resistance ensues.



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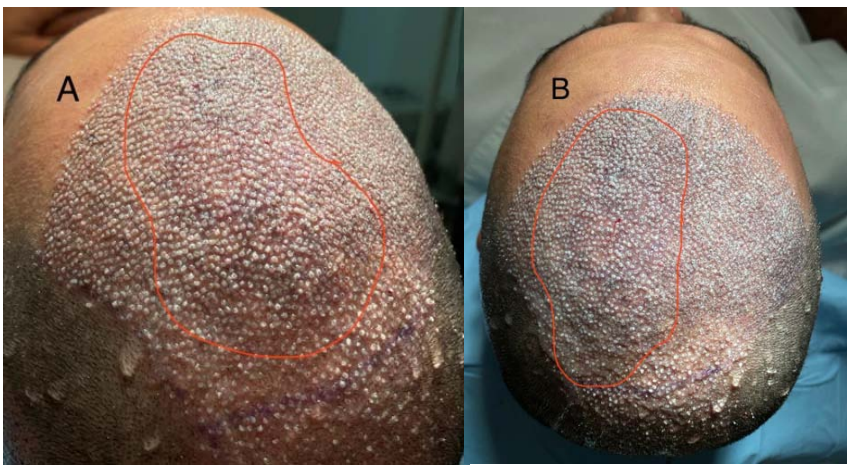
Picture 4: Tissue with reddish coloring indicating blood flow and mature collagen (A) and (B). There was hair growth of some follicles implanted in the area, which demonstrates recovery from the hair transplant through ozone therapy (C) and (D)

For data collection, pictures after hair transplantation procedure (Picture 5). High density and dark coloring areas due to possible ischemia are visible.



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Picture 5: Hair transplant with high approximation of FUs in (A) and (B) showing spots with immediate reduction of blood flow

There is limited evidence on the direct use of ozone therapy in hair transplantation, but it is successful in several other treatments and it presents a therapeutic challenge. There are several therapies for dermal treatment but their adverse effects hamper their application. However, as previously observed, ozone therapy, despite being a simple molecule, holds an

efficient approach to fight microorganisms and promote healing capacity.

V. Conclusion

The current study demonstrated the use of ozone for ischemic tissue treatment. Eventual therapeutic outcomes were positive as healing evolution was attested as a result of improved blood flow and re-epithelialization of damaged tissue.

Despite being an innovative procedure, hair transplantation does not exclude the possibility of necrosis, which highlights the importance of the availability of tools to cope with unexpected situations. Healing is a complex process and demands immediate intervention in face of its occurrence.

This case report is free of any conflict of interest and aims at supporting study and learning initiatives by professionals addressing similar cases in their professional settings.

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10. Use proper verb tense: Use proper verb tenses in your paper. Use past tense to present those events that have happened. Use present tense to indicate events that are going on. Use future tense to indicate events that will happen in the future. Use of wrong tenses will confuse the evaluator. Avoid sentences that are incomplete.

11. Pick a good study spot: Always try to pick a spot for your research which is quiet. Not every spot is good for studying.

12. Know what you know: Always try to know what you know by making objectives, otherwise you will be confused and unable to achieve your target.

13. Use good grammar: Always use good grammar and words that will have a positive impact on the evaluator; use of good vocabulary does not mean using tough words which the evaluator has to find in a dictionary. Do not fragment sentences. Eliminate one-word sentences. Do not ever use a big word when a smaller one would suffice.

Verbs have to be in agreement with their subjects. In a research paper, do not start sentences with conjunctions or finish them with prepositions. When writing formally, it is advisable to never split an infinitive because someone will (wrongly) complain. Avoid clichés like a disease. Always shun irritating alliteration. Use language which is simple and straightforward. Put together a neat summary.

14. Arrangement of information: Each section of the main body should start with an opening sentence, and there should be a changeover at the end of the section. Give only valid and powerful arguments for your topic. You may also maintain your arguments with records.

15. Never start at the last minute: Always allow enough time for research work. Leaving everything to the last minute will degrade your paper and spoil your work.

16. Multitasking in research is not good: Doing several things at the same time is a bad habit in the case of research activity. Research is an area where everything has a particular time slot. Divide your research work into parts, and do a particular part in a particular time slot.

17. Never copy others' work: Never copy others' work and give it your name because if the evaluator has seen it anywhere, you will be in trouble. Take proper rest and food: No matter how many hours you spend on your research activity, if you are not taking care of your health, then all your efforts will have been in vain. For quality research, take proper rest and food.

18. Go to seminars: Attend seminars if the topic is relevant to your research area. Utilize all your resources.

19. Refresh your mind after intervals: Try to give your mind a rest by listening to soft music or sleeping in intervals. This will also improve your memory. Acquire colleagues: Always try to acquire colleagues. No matter how sharp you are, if you acquire colleagues, they can give you ideas which will be helpful to your research.

20. Think technically: Always think technically. If anything happens, search for its reasons, benefits, and demerits. Think and then print: When you go to print your paper, check that tables are not split, headings are not detached from their descriptions, and page sequence is maintained.

21. Adding unnecessary information: Do not add unnecessary information like "I have used MS Excel to draw graphs." Irrelevant and inappropriate material is superfluous. Foreign terminology and phrases are not apropos. One should never take a broad view. Analogy is like feathers on a snake. Use words properly, regardless of how others use them. Remove quotations. Puns are for kids, not grunt readers. Never oversimplify: When adding material to your research paper, never go for oversimplification; this will definitely irritate the evaluator. Be specific. Never use rhythmic redundancies. Contractions shouldn't be used in a research paper. Comparisons are as terrible as clichés. Give up ampersands, abbreviations, and so on. Remove commas that are not necessary. Parenthetical words should be between brackets or commas. Understatement is always the best way to put forward earth-shaking thoughts. Give a detailed literary review.

22. Report concluded results: Use concluded results. From raw data, filter the results, and then conclude your studies based on measurements and observations taken. An appropriate number of decimal places should be used. Parenthetical remarks are prohibited here. Proofread carefully at the final stage. At the end, give an outline to your arguments. Spot perspectives of further study of the subject. Justify your conclusion at the bottom sufficiently, which will probably include examples.

23. Upon conclusion: Once you have concluded your research, the next most important step is to present your findings. Presentation is extremely important as it is the definite medium though which your research is going to be in print for the rest of the crowd. Care should be taken to categorize your thoughts well and present them in a logical and neat manner. A good quality research paper format is essential because it serves to highlight your research paper and bring to light all necessary aspects of your research.

Informal Guidelines of Research Paper Writing

Key points to remember:

- Submit all work in its final form.
- Write your paper in the form which is presented in the guidelines using the template.
- Please note the criteria peer reviewers will use for grading the final paper.

Final points:

One purpose of organizing a research paper is to let people interpret your efforts selectively. The journal requires the following sections, submitted in the order listed, with each section starting on a new page:

The introduction: This will be compiled from reference matter and reflect the design processes or outline of basis that directed you to make a study. As you carry out the process of study, the method and process section will be constructed like that. The results segment will show related statistics in nearly sequential order and direct reviewers to similar intellectual paths throughout the data that you gathered to carry out your study.

The discussion section:

This will provide understanding of the data and projections as to the implications of the results. The use of good quality references throughout the paper will give the effort trustworthiness by representing an alertness to prior workings.

Writing a research paper is not an easy job, no matter how trouble-free the actual research or concept. Practice, excellent preparation, and controlled record-keeping are the only means to make straightforward progression.

General style:

Specific editorial column necessities for compliance of a manuscript will always take over from directions in these general guidelines.

To make a paper clear: Adhere to recommended page limits.

Mistakes to avoid:

- Insertion of a title at the foot of a page with subsequent text on the next page.
- Separating a table, chart, or figure—confine each to a single page.
- Submitting a manuscript with pages out of sequence.
- In every section of your document, use standard writing style, including articles ("a" and "the").
- Keep paying attention to the topic of the paper.
- Use paragraphs to split each significant point (excluding the abstract).
- Align the primary line of each section.
- Present your points in sound order.
- Use present tense to report well-accepted matters.
- Use past tense to describe specific results.
- Do not use familiar wording; don't address the reviewer directly. Don't use slang or superlatives.
- Avoid use of extra pictures—include only those figures essential to presenting results.

Title page:

Choose a revealing title. It should be short and include the name(s) and address(es) of all authors. It should not have acronyms or abbreviations or exceed two printed lines.

Abstract: This summary should be two hundred words or less. It should clearly and briefly explain the key findings reported in the manuscript and must have precise statistics. It should not have acronyms or abbreviations. It should be logical in itself. Do not cite references at this point.

An abstract is a brief, distinct paragraph summary of finished work or work in development. In a minute or less, a reviewer can be taught the foundation behind the study, common approaches to the problem, relevant results, and significant conclusions or new questions.

Write your summary when your paper is completed because how can you write the summary of anything which is not yet written? Wealth of terminology is very essential in abstract. Use comprehensive sentences, and do not sacrifice readability for brevity; you can maintain it succinctly by phrasing sentences so that they provide more than a lone rationale. The author can at this moment go straight to shortening the outcome. Sum up the study with the subsequent elements in any summary. Try to limit the initial two items to no more than one line each.

Reason for writing the article—theory, overall issue, purpose.

- Fundamental goal.
- To-the-point depiction of the research.
- Consequences, including definite statistics—if the consequences are quantitative in nature, account for this; results of any numerical analysis should be reported. Significant conclusions or questions that emerge from the research.

Approach:

- Single section and succinct.
- An outline of the job done is always written in past tense.
- Concentrate on shortening results—limit background information to a verdict or two.
- Exact spelling, clarity of sentences and phrases, and appropriate reporting of quantities (proper units, important statistics) are just as significant in an abstract as they are anywhere else.

Introduction:

The introduction should "introduce" the manuscript. The reviewer should be presented with sufficient background information to be capable of comprehending and calculating the purpose of your study without having to refer to other works. The basis for the study should be offered. Give the most important references, but avoid making a comprehensive appraisal of the topic. Describe the problem visibly. If the problem is not acknowledged in a logical, reasonable way, the reviewer will give no attention to your results. Speak in common terms about techniques used to explain the problem, if needed, but do not present any particulars about the protocols here.

The following approach can create a valuable beginning:

- Explain the value (significance) of the study.
- Defend the model—why did you employ this particular system or method? What is its compensation? Remark upon its appropriateness from an abstract point of view as well as pointing out sensible reasons for using it.
- Present a justification. State your particular theory(-ies) or aim(s), and describe the logic that led you to choose them.
- Briefly explain the study's tentative purpose and how it meets the declared objectives.

Approach:

Use past tense except for when referring to recognized facts. After all, the manuscript will be submitted after the entire job is done. Sort out your thoughts; manufacture one key point for every section. If you make the four points listed above, you will need at least four paragraphs. Present surrounding information only when it is necessary to support a situation. The reviewer does not desire to read everything you know about a topic. Shape the theory specifically—do not take a broad view.

As always, give awareness to spelling, simplicity, and correctness of sentences and phrases.

Procedures (methods and materials):

This part is supposed to be the easiest to carve if you have good skills. A soundly written procedures segment allows a capable scientist to replicate your results. Present precise information about your supplies. The suppliers and clarity of reagents can be helpful bits of information. Present methods in sequential order, but linked methodologies can be grouped as a segment. Be concise when relating the protocols. Attempt to give the least amount of information that would permit another capable scientist to replicate your outcome, but be cautious that vital information is integrated. The use of subheadings is suggested and ought to be synchronized with the results section.

When a technique is used that has been well-described in another section, mention the specific item describing the way, but draw the basic principle while stating the situation. The purpose is to show all particular resources and broad procedures so that another person may use some or all of the methods in one more study or referee the scientific value of your work. It is not to be a step-by-step report of the whole thing you did, nor is a methods section a set of orders.

Materials:

Materials may be reported in part of a section or else they may be recognized along with your measures.

Methods:

- Report the method and not the particulars of each process that engaged the same methodology.
- Describe the method entirely.
- To be succinct, present methods under headings dedicated to specific dealings or groups of measures.
- Simplify—detail how procedures were completed, not how they were performed on a particular day.
- If well-known procedures were used, account for the procedure by name, possibly with a reference, and that's all.

Approach:

It is embarrassing to use vigorous voice when documenting methods without using first person, which would focus the reviewer's interest on the researcher rather than the job. As a result, when writing up the methods, most authors use third person passive voice.

Use standard style in this and every other part of the paper—avoid familiar lists, and use full sentences.

What to keep away from:

- Resources and methods are not a set of information.
- Skip all descriptive information and surroundings—save it for the argument.
- Leave out information that is immaterial to a third party.

Results:

The principle of a results segment is to present and demonstrate your conclusion. Create this part as entirely objective details of the outcome, and save all understanding for the discussion.

The page length of this segment is set by the sum and types of data to be reported. Use statistics and tables, if suitable, to present consequences most efficiently.

You must clearly differentiate material which would usually be incorporated in a study editorial from any unprocessed data or additional appendix matter that would not be available. In fact, such matters should not be submitted at all except if requested by the instructor.

Content:

- Sum up your conclusions in text and demonstrate them, if suitable, with figures and tables.
- In the manuscript, explain each of your consequences, and point the reader to remarks that are most appropriate.
- Present a background, such as by describing the question that was addressed by creation of an exacting study.
- Explain results of control experiments and give remarks that are not accessible in a prescribed figure or table, if appropriate.
- Examine your data, then prepare the analyzed (transformed) data in the form of a figure (graph), table, or manuscript.

What to stay away from:

- Do not discuss or infer your outcome, report surrounding information, or try to explain anything.
- Do not include raw data or intermediate calculations in a research manuscript.
- Do not present similar data more than once.
- A manuscript should complement any figures or tables, not duplicate information.
- Never confuse figures with tables—there is a difference.

Approach:

As always, use past tense when you submit your results, and put the whole thing in a reasonable order.

Put figures and tables, appropriately numbered, in order at the end of the report.

If you desire, you may place your figures and tables properly within the text of your results section.

Figures and tables:

If you put figures and tables at the end of some details, make certain that they are visibly distinguished from any attached appendix materials, such as raw facts. Whatever the position, each table must be titled, numbered one after the other, and include a heading. All figures and tables must be divided from the text.

Discussion:

The discussion is expected to be the trickiest segment to write. A lot of papers submitted to the journal are discarded based on problems with the discussion. There is no rule for how long an argument should be.

Position your understanding of the outcome visibly to lead the reviewer through your conclusions, and then finish the paper with a summing up of the implications of the study. The purpose here is to offer an understanding of your results and support all of your conclusions, using facts from your research and generally accepted information, if suitable. The implication of results should be fully described.

Infer your data in the conversation in suitable depth. This means that when you clarify an observable fact, you must explain mechanisms that may account for the observation. If your results vary from your prospect, make clear why that may have happened. If your results agree, then explain the theory that the proof supported. It is never suitable to just state that the data approved the prospect, and let it drop at that. Make a decision as to whether each premise is supported or discarded or if you cannot make a conclusion with assurance. Do not just dismiss a study or part of a study as "uncertain."

Research papers are not acknowledged if the work is imperfect. Draw what conclusions you can based upon the results that you have, and take care of the study as a finished work.

- You may propose future guidelines, such as how an experiment might be personalized to accomplish a new idea.
- Give details of all of your remarks as much as possible, focusing on mechanisms.
- Make a decision as to whether the tentative design sufficiently addressed the theory and whether or not it was correctly restricted. Try to present substitute explanations if they are sensible alternatives.
- One piece of research will not counter an overall question, so maintain the large picture in mind. Where do you go next? The best studies unlock new avenues of study. What questions remain?
- Recommendations for detailed papers will offer supplementary suggestions.

Approach:

When you refer to information, differentiate data generated by your own studies from other available information. Present work done by specific persons (including you) in past tense.

Describe generally acknowledged facts and main beliefs in present tense.

The Administration Rules

Administration Rules to Be Strictly Followed before Submitting Your Research Paper to Global Journals Inc.

Please read the following rules and regulations carefully before submitting your research paper to Global Journals Inc. to avoid rejection.

Segment draft and final research paper: You have to strictly follow the template of a research paper, failing which your paper may get rejected. You are expected to write each part of the paper wholly on your own. The peer reviewers need to identify your own perspective of the concepts in your own terms. Please do not extract straight from any other source, and do not rephrase someone else's analysis. Do not allow anyone else to proofread your manuscript.

Written material: You may discuss this with your guides and key sources. Do not copy anyone else's paper, even if this is only imitation, otherwise it will be rejected on the grounds of plagiarism, which is illegal. Various methods to avoid plagiarism are strictly applied by us to every paper, and, if found guilty, you may be blacklisted, which could affect your career adversely. To guard yourself and others from possible illegal use, please do not permit anyone to use or even read your paper and file.

Criterion for Grading a Research Paper (Compilation) by Global Journals

Please note that following table is only a Grading of "Paper Compilation" and not on "Performed/Stated Research" whose grading solely depends on Individual Assigned Peer Reviewer and Editorial Board Member. These can be available only on request and after decision of Paper. This report will be the property of Global Journals.

Topics	Grades		
	A-B	**C-D**	**E-F**
Abstract	Clear and concise with appropriate content, Correct format. 200 words or below	Unclear summary and no specific data, Incorrect form Above 200 words	No specific data with ambiguous information Above 250 words
Introduction	Containing all background details with clear goal and appropriate details, flow specification, no grammar and spelling mistake, well organized sentence and paragraph, reference cited	Unclear and confusing data, appropriate format, grammar and spelling errors with unorganized matter	Out of place depth and content, hazy format
Methods and Procedures	Clear and to the point with well arranged paragraph, precision and accuracy of facts and figures, well organized subheads	Difficult to comprehend with embarrassed text, too much explanation but completed	Incorrect and unorganized structure with hazy meaning
Result	Well organized, Clear and specific, Correct units with precision, correct data, well structuring of paragraph, no grammar and spelling mistake	Complete and embarrassed text, difficult to comprehend	Irregular format with wrong facts and figures
Discussion	Well organized, meaningful specification, sound conclusion, logical and concise explanation, highly structured paragraph reference cited	Wordy, unclear conclusion, spurious	Conclusion is not cited, unorganized, difficult to comprehend
References	Complete and correct format, well organized	Beside the point, Incomplete	Wrong format and structuring

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