INVESTIGATION OF PAEDERIA FOETIDA TOWARDS THE FERTILITY IN EARLY POST IMPLANTATION

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by

REENA SHARMA

(Roll No. - 2202270986005)

Under the Supervision of

Dr. Amarjeet Singh
(Principal, Innovative College of Pharmacy, Greater Noida)
&
Co-guide
Mrs. Reenu Tiwari
(Assistant Professor, Innovative College of Pharmacy, Greater Noida)

to the
Faculty of Pharmacy

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REENA SHARMA

ABSTRACT

Female infertility represents a significant challenge in human reproduction, impacting countless individuals worldwide. This complex disorder, characterized by an inability to conceive or carry a pregnancy to term, stems from a multitude of factors in our modern world. The increasing prevalence of infertility can be attributed to various elements of contemporary life, including heightened stress levels, excessive exposure to radiation, consumption of non-organic foods, genetic predispositions, evolving lifestyles, and the pervasive presence of electronic devices emitting electromagnetic fields.

The personal toll of infertility or childlessness is profound, often resulting in deep emotional distress and suffering. Much of this anguish remains concealed from public view, contributing to the societal taboo surrounding open discussions of fertility struggles.

At its core, female fertility relies on the intricate interplay of hormones within the hypothalamic-pituitary-ovarian axis. Disruptions to this delicate balance can occur at any point in this system, potentially compromising ovulation. Additionally, physical issues such as endometriosis or infections can distort or obstruct the fallopian tubes, further complicating conception. It's also worth noting that the quality of ova and the likelihood of spontaneous pregnancy naturally decline with age.

This comprehensive review delves into the traditional medicinal applications, phytochemical composition, pharmacological properties, toxicological profile, and clinical studies of two plant species: Paederiafoetida and Paederia scandens. Phytochemical analyses have revealed these plants contain a rich array of compounds, including iridoids, flavonoids, volatile oils, and other metabolites, suggesting potential therapeutic properties.

The study aims to explore alternative approaches to addressing infertility, with a focus on these medicinal plants. It also examines contemporary techniques and interventions used in fertility treatment. By bridging traditional knowledge with modern scientific understanding, this research seeks to offer new perspectives and potential solutions for those grappling with infertility.

Through this holistic approach, the study not only contributes to the scientific understanding of these plants but also offers hope to those seeking diverse options in their fertility journey. It underscores the importance of considering both traditional wisdom and cutting-edge medical advancements in addressing the complex issue of female infertility.

Keywords: Infertility,Endrometrosis,Paederiafoetida,Iridoids, Albino rats etc.

DECLARATION

I hereby declare that the work presented in this report entitled "**INVESTIGATION OF PAEDERIA FOETIDA TOWARDS THE FERTILITY IN EARLY POST IMPLANTATION**", was carried out by me. I have not submitted the matter embodied in this report for the award of any other degree or diploma of any other University or Institute. I have given due credit to the original authors/sources for all the words, ideas, diagrams, graphics, computer programs, experiments, results, that are not my original contribution. I have used quotation marks to identify verbatim sentences and given credit to the original authors/sources. I affirm that no portion of my work is plagiarized, and the experiments and results reported in the report are not manipulated. In the event of a complaint of plagiarism and the manipulation of the experiments and results, I shall be fully responsible and answerable.

Name : Reena Sharma

Roll. No. : 2202270986005

Branch : Pharmacology

(Candidate Signature)

CHAPTER-1

INTRODUCTION

Infertility is a condition where a couple fails to achieve pregnancy after engaging in consistent,unprotected sexual intercourse over a defined timeframe: usually 12 months for women under 35and 6 months for women 35 and older. It also encompasses the inability to sustain a pregnancy tofull term, resulting in recurrent pregnancy loss or stillbirth. Infertility may stem from problems ineither partner or a combination of both and is influenced by various biological, medical, lifestyle,andenvironmentalfactors[27].

1.1 TYPESOFINFERTILITY

Infertilitymanifestsinseveraldistinctforms:

1.1.1 PrimaryInfertility

Primary infertility refers to the situation where a couple is unable to conceive after engaging inregular, unprotected sexual intercourse for a year, or for six months if the woman is 35 or older,with no history of previous pregnancies. This form of infertility indicates that neither partner hasbeenable tosuccessfullyachieve pregnancybefore,despite activeefforts[8].

1.1.2 SecondaryInfertility

Secondaryinfertilityoccurswhenacouple,whohaspreviouslyexperiencedatleastonesuccessfulpregnancy, finds themselves unable to conceive again despite continuous, unprotected sexualactivity over a specified duration (typically a year). This type of infertility can arise even if theyhadnodifficultyconceivinginthepastorifpreviouspregnanciesendedinlivebirths,miscarriages,or stillbirths[46].

1.1.3 UnexplainedInfertility

Unexplained infertility describes a scenario where a couple's or individual's infertility remainsundiagnosed after comprehensive fertility evaluations. Despite thorough testing and analysis ofreproductive health, no clear cause for the inability to conceive has been identified. This
categoryofinfertilityhighlightscaseswhereconventionalmedicalassessmentscannotpinpointadefinitivereason forthereproductive difficulties,leavingtheunderlyingissuesunknown[33].

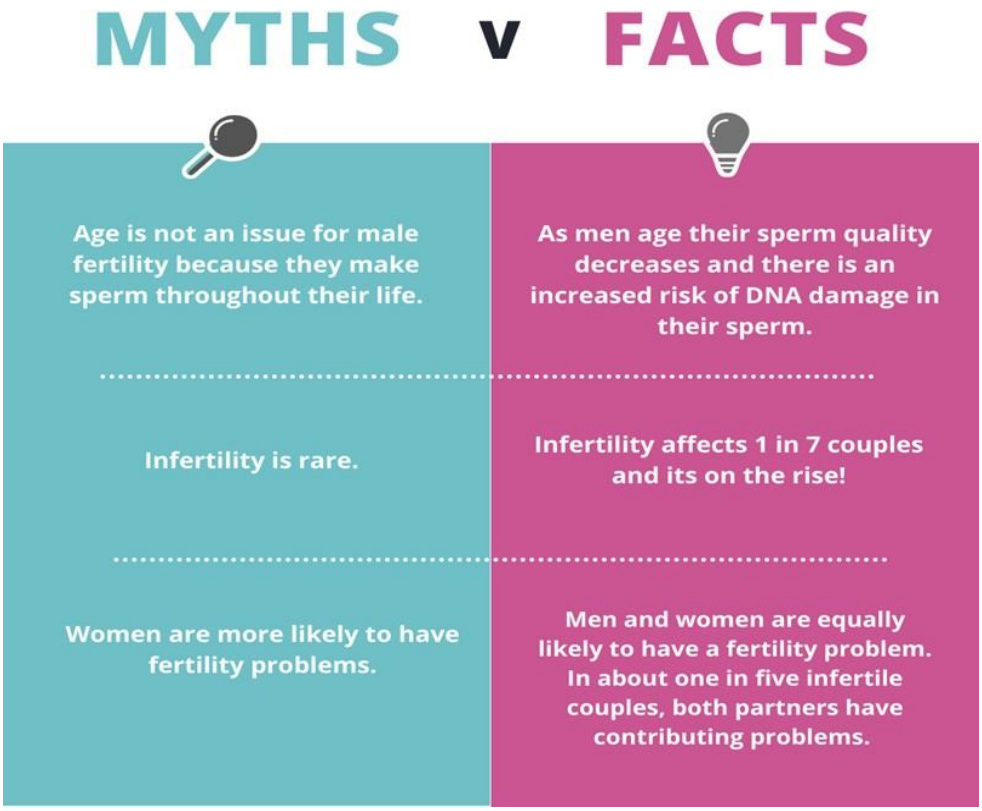

Fig.1.1FactsandMythaboutInfertility

1.2 REASONS WHYWOMENAREINFERTILE

1.2.1 Ovulationdisorders:

Ovulation disorders significantly contribute to women's fertility issues, encompassing severalconditions that impair normal ovarian function. These include hormonal imbalances like PCOS,characterized by excess male hormones and metabolic issues, often leading to inconsistent orabsenteggrelease.Brain-ovarycommunicationdisruptions,triggeredbystressorlifestylefactors,can cause menstrual and ovulation irregularities. Premature loss of ovarian function before 40,potentially stemming from genetic or immune system problems, also impacts fertility. Lifestylechoices play a role too: intense physical activity can halt menstruation, extreme weight loss maysuppress reproduction, and obesity can boost estrogen, interfering with ovulation. These issuesillustrate the sensitive hormonal equilibrium needed for regular egg release and demonstrate howcloselyreproductivehealthistiedtooverallbodyfunction[12].

1.2.2 Fallopiantubedamageorblockage:

Fallopian tube issues are a significant cause of female infertility. These delicate structures can bedamagedorblockedbyvariousfactors.Pelvicinflammatorydisease,oftenresultingfromsexuallytran smittedinfections,cancausescarringthatobstructsthetubes.Ahistoryofectopicpregnancy,

where the embryo implants outside the uterus, typically in a fallopian tube, can lead to tubedamage.Endometriosis,aconditionwhereuterineliningtissuegrowsoutsidetheuterus,canaffectthe tubes, causing blockages or adhesions. Additionally, previous abdominal or pelvic surgeriesmay result in scar tissue formation, potentially leading to tubal adhesions. These obstructions ordamagescanpreventtheeggandspermfrommeeting,orhinderthefertilizedegg'sjourneytotheuterus,t husimpactingfertility[58].

1.2.3 Endometriosis:

Endometriosis and uterine or cervical abnormalities can significantly impact female fertility.Endometriosis occurs when uterine tissue grows outside the uterus, potentially affecting ovaries,fallopiantubes,andembryoimplantation.Uterineandcervicalissuesencompassvariousconditi ons:congenitaldefectslikeaseptateuterusdividetheuterinecavity,potentiallyinterferingwithimplantat ion.Uterinefibroidsorpolyps,benigngrowthsintheuterus,candisrupttheuterineenvironment.

Cervical stenosis, a narrowing of the cervix, may impede sperm entry or menstrualflow.Asherman'ssyndrome,characterizedbyuterineadhesions,canresultfromuterineproce duresandaffectimplantation.Theseconditionscaninterferewithconceptionandpregnancymaintenanc e,contributingtofertilitychallenges[35].

1.2.4 Primaryovarianinsufficiency:

Primary ovarian insufficiency, also known as premature ovarian failure, is a condition where awoman's ovaries cease functioning normally before the age of 40. This disorder is characterizedby an early depletion of the ovarian reserve, which is the pool of eggs available for reproduction.The causes of this condition are diverse and can include genetic factors, such as chromosomalabnormalities or specific gene mutations. Medical treatments like chemotherapy or radiationtherapyforcancercanalsodamageovariantissue,leadingtoinsufficiency.Additionally,autoi mmune disordersmay cause thebody to mistakenly attack ovarian tissue,resultinginpremature egg depletion. This condition significantly impacts fertility, often leading to irregularorabsentmenstrualcycles anddifficultyconceivingnaturally[40].

1.2.5 Uterineorcervicalabnormalities:

Uterineandcervicalabnormalitiescansignificantlyimpactfertilityandpregnancy.Theseincludeconge nital defects such as aseptate uterus,where theuterus is partially divided.Acquiredconditionslikeuterinefibroidsorpolypscanalsoposechallenges.Cervicalstenosis,ch aracterizedby a narrowing of the cervical opening, may impede sperm entry or menstrual flow. Asherman'ssyndrome,involvingadhesionswithintheuterus,caninterferewithimplantationandfetalde velopment.Theseconditionsmayrequiremedicalinterventiontoimprovereproductiveoutcomes[53].

1.2.6 ThyroidProblems:

Thyroiddisorderscanhaveasignificantimpactonfertility.Bothhyperthyroidism(overactive

thyroid)andhypothyroidism(underactivethyroid)candisruptthenormalovulationprocess.Thesecondi tions affect the production and regulation of hormones that are crucial for reproductivefunction. As a result, women with thyroid problems may experience irregular menstrual cycles,anovulation (lack of ovulation), or difficulties conceiving. Proper diagnosis and management ofthyroid disordersareessential foroptimizingfertilityand supportinghealthypregnancies[19].

1.2.7 AgeRelatedfactor:

Age-related factors play a crucial role in female fertility. As women age, particularly after 35,there's a notable decline in both the quality and quantity of their eggs. This natural process, oftenreferred to as diminished ovarian reserve, can significantly impact a woman's ability to conceive.The remaining eggs are more likely to have chromosomal abnormalities, increasing the risk ofmiscarriage or genetic disorders in offspring. This biological reality underscores the importanceofconsideringagewhenplanningforpregnancyoraddressingfertilityconcerns[49].

1.2.8 HormonalImbalances:

Hormonal imbalances can significantly impact female fertility. Two notable conditions are lutealphase defect and hyperprolactinemia. In luteal phase defect, there's inadequate production ofprogesterone, a hormone crucial for maintaining pregnancy in its early stages. This can lead todifficulties in implantation or early pregnancy loss. Hyperprolactinemia, characterized by excessproductionofprolactin,caninterferewithnormalovulationandmenstrualcycles.Bothconditions can disrupt the delicate hormonal balance necessary for successful conception and pregnancy,oftenrequiringmedicalinterventionforpropermanagementandimprovedfertilityoutcome s[4].

1.2.9 GeneticFactor:

Geneticfactorsplayasignificantroleinfertilityandreproductivehealth.Chromosomalabnormalities, which involve changes in the structure or number of chromosomes, can lead toinfertility, recurrent miscarriages, or birth defects. Additionally, individuals may be carriers ofgenetic disorders without showing symptoms themselves. When both partners carry the samerecessive gene mutation, there's a risk of passing the disorder to their offspring. These geneticfactors can impact fertility, pregnancy outcomes, and the health of future children, highlightingthe importance ofgeneticcounselingandtestinginreproductive planning[29].

1.2.10 AutoImmuneDisorder:

Autoimmune disorders can have a significant impact on fertility. Conditions such as lupus andrheumatoid arthritis, where the immune system mistakenly attacks the body's own tissues, caninterferewithreproductivefunction.Thesedisordersmayaffectovarianreserve,disrupt hormonebalance, or increase the risk of pregnancy complications. Additionally, some medications used totreat autoimmune conditions can temporarily impact fertility. The complex interplay between

theimmunesystemandreproductivehealthinthesedisordersoftenrequirescarefulmanagementandcoordinationbetweenrheumatologistsandfertilityspecialiststooptimizechancesofconception

andhealthypregnancyoutcomes[6].

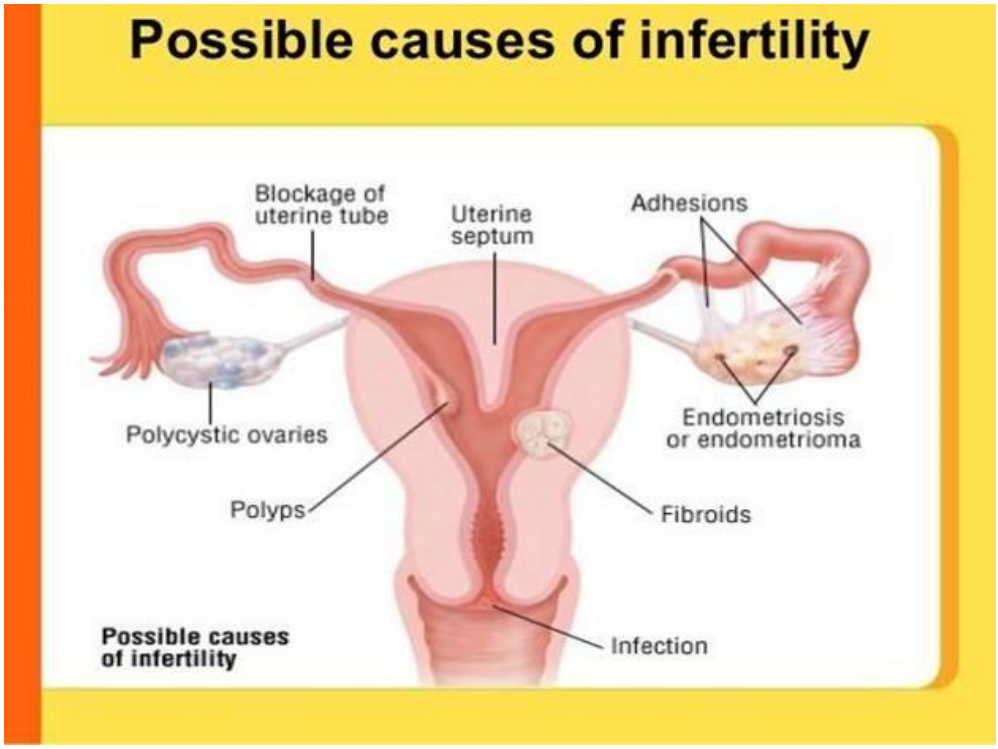

Fig.1.2Possiblecausesofinfertility

1.3 INDICATIONSANDSIGNSOFPOSSIBLEINFERTILEWOMEN

Variations in the menstrual cycle and ovulation can be important indicators of potential fertilityissuesinwomen.Thesesymptomsoftensignalunderlyingconditionsthatmayaffectreproductivehealth.Here's a detailedbreakdownofthesesigns:

1. UnusualMenstrualFlow:

- Heavierthannormalbleeding(menorrhagia)canindicatehormonalimbalances,uterinefibroids,or endometriosis.
- Lighterthanusualflowmightsuggestlowestrogenlevels orconditionslikepolycysticovarysyndrome (PCOS)[44].

2. IrregularMenstrualCycle:

- Inconsistentintervalsbetweenperiods(varyingbymorethanafewdayseachmonth)cansignalhormonalimbalances orovulationdisorders.
- Thisirregularitymayaffectfertilitybymaking itdifficulttopredictovulation[2].

3. AbsenceofPeriods(Amenorrhea):

- Primaryamenorrhea:never havinghadaperiodbyage16.

- Secondaryamenorrhea:thecessationofperiods forthreeor moreconsecutivemonths.
- CanbecausedbyconditionslikePCOS,prematureovarianfailure,orextremestress[15].

4. PainfulPeriods(Dysmenorrhea):

- Severecramping,pelvicpain,andbackpainduring menstruation.
- Mayindicateconditionslikeendometriosis,uterine fibroids,orpelvic inflammatorydisease[34].

5. SkinChanges:

- Increasedacne,particularlyinadulthood,cansignalhormonalimbalanceslikeelevatedandrogens.
- OftenassociatedwithconditionslikePCOS.

6. AlterationsinLibido:

- Changesinsexdrivecanbe linkedtohormonalimbalancesaffecting fertility.
- Bothincreasedanddecreasedlibidomaybesignsofunderlyingissues[36].

7. Hirsutism:

- Excessivedarkhairgrowthontheface, chest, andlips.
- Oftenindicateselevatedandrogenlevels, asseeninPCOS[56].

8. HairThinningorBaldness:

- Femalepatternhairlosscanbeasignofhormonalimbalancesaffectingfertility.
- Mayberelated tothyroiddisordersorotherendocrineissues[2].

9. WeightGain:

- Unexplainedweight gain,especiallyaroundthemidsection.
- CanbeassociatedwithPCOS,thyroiddisorders,orother hormonalimbalances[15].

10. Galactorrhea:

- Milkywhitedischargefromnipplesunrelatedtopregnancyorbreastfeeding.
- Mayindicateelevatedprolactinlevels,whichcaninterferewithovulation[47].

11. Dyspareunia(PainDuringIntercourse):

- Can be caused by conditionslike endometriosis,pelvicinflammatory disease,or hormonalimbalancesleadingtovaginaldryness.
- Mayaffectsexualfrequencyandtiming,impactingconceptionchances[56].

Fig.1.3Indicationsandsignsofinfertility

1.4 DIAGNOSTICTESTFORINFERTILITY

1.4.1 BloodExaminations

Progesterone levels in the blood can indicate whether ovulation is occurring. The timing of thistest is based on the regularity of your menstrual cycle. For those with irregular periods, a test tomeasuregonadotrophins(hormonesthatstimulatetheovariestoproduceeggs)mayberecommended[41].

1.4.2 UrinaryLuteinizingHormone(LH)

Over-the-counter "ovulation predictor kits" can measure LH levels in urine, detecting a surge inthishormonethathappens1-2daysbeforeovulation.Unlikebloodprogesteronetests,urinaryLHtests can predict ovulation. The most fertile period, identified by these tests, is the day of the LHsurge and the following two days. Due to the cost, these tests are best for women with menstrualcyclesconsistentlylastingbetween25and35days[25].

1.4.3 Sonohysterography

This procedure involves filling the uterus with saline (a salt solution) and using transvaginalultrasound to detect intrauterine issues such as endometrial polyps and fibroids more effectivelythantransvaginalultrasoundalone.Ifanabnormalityisfound,ahysteroscopyisusuallyperformed. Sonohysterography often replaces HSG (hysterosalpingography) for detecting suchissues[14].

1.4.4 TransvaginalUltrasonography

By inserting an ultrasound probe into the vagina, this procedure allows a healthcare provider toexaminethe uterusandovariesforabnormalitieslike ovariancystsandfibroids[22].

1.4.5 EndometrialBiopsy

A specialist takes a sample of the endometrial lining of the uterus after ovulation, testing it forsigns of inflammation, hormonal changes, and ovulation-related changes. This test is typicallyperformed 7-12 days post-ovulation. However, it is rarely used today for diagnosing or treatinginfertility. An endometrial biopsy is necessary for the Endometrial Receptivity Assay (ERA),whichsometimesaimstodeterminethebestday totransferanembryoinanIVFcycle.Unfortunately,thereis noevidencethatthistestimprovespregnancychances formostwomen[1].

1.4.6 X-ray

AhysterosalpingograminvolvestakinganX-rayofthefallopiantubesandwombafterinjectingaspecial dye. This test can identify blockages in the fallopian tubes that might prevent eggs fromreachingthewomb[51].

1.4.7 Laparoscopy

Laparoscopy,orkeyholesurgery,involvesmakingasmallincisioninthelowerabdomentoinsertalaparo scope—athintubewithacamera—toinspecttheovaries,fallopiantubes,andwomb.Dyecan be injected through the cervix to highlight any tube obstructions. This procedure is usuallyreserved for cases with a high risk of complications, such as a history of pelvic inflammatorydisease (PID)orsuspectedtube blockagebasedonscans[30].

1.4.8 UltrasoundExamination

An ultrasound scan can examine the fallopian tubes, uterus, and ovaries. Conditions like fibroidsand endometriosis, which can prevent pregnancy, can be identified. The scan can also look forsigns of potential blockage in the fallopian tubes, which might prevent eggs from reaching thewomb. If a possible blockage is detected, your doctor may refer you to a specialist for furthertesting,suchaslaparoscopy[10.]

1.5 ASSISTEDREPRODUCTIVETECHNOLOGY

Ifpregnancydoesnotoccurafterayearofregular,unprotectedintercourse,aninfertilityevaluationbegins . In some situations, such as a history of amenorrhea (absence of menstruation), it may beappropriatetostarttheevaluationsooner.Bothpartnerstypicallyundergosimultaneous infertilityassessmentsatageneralmedicalfacility,whereanursewilldocumenttheirsexualandgynecolo gicalhistory[42].

Couples undergo medical evaluations to identify the cause of their infertility before startingtreatment.Treatmentplansarethentailoredtothecouple'spreferencesandneeds,consideringthewoman'sageandtheunderlyingcausesofinfertility.Beforeinitiatingany treatment,itiscrucialtodiscussalternativeoptionsandthepossibilityofunsuccessfuloutcomesopenly.

Common treatments include hormonal therapy, surgery (to address endometriosis and fibroids),and assisted reproductive technologies such as artificial insemination and in vitro fertilization(IVF)[11].

1.5.1 IVF(InVitroFertilization)

In Vitro Fertilization (IVF) involves combining an egg and sperm outside the body. The processincludesmonitoringandstimulatingawoman'sovulatorycycle,retrievingeggsfromherovaries,andallowingspermtofertilizetheminalabculturemedium.Theresulting fertilizedegg(zygote)isthenculturedfortwotosixdaysbeforebeingtransferredintotheuterusviaacathetertoestablisha pregnancy[55].

- **Superovulation and Stimulation:** Typically, a woman releases one egg per month.However,forIVF,medicationsareprescribedtostimulatetheovariestoproducemultipleeggs inacycle.Theseeggsaremonitoredtoselectthehealthiestones forthenextsteps.
- **Egg Retrieval and Sperm Processing:** Eggs are extracted from the woman through aprocess called transvaginal oocyte retrieval. The best eggs are identified using oocyteselection. Sperm washing is used to remove seminal fluid and inactive cells, isolating thesperm.
- **Egg Fertilization:** The selected sperm and egg are incubated together for fertilization.Usually, the sperm penetrates the egg naturally, but in cases of low sperm motility, thespermmaybeinjecteddirectlyintotheegg.
- **Embryo Development:** The fertilized egg begins to divide and develop into an embryo.Afterfivetosixdaysofincubation,theembryoreachestheblastocyststage.
- **Embryo Transfer:** The embryo is transferred to the uterus after five to six days ofdevelopment. The number of embryos transferred depends on the woman's age and anyexisting health conditions. A catheter is used to place the embryos into the womb throughthecervixandvagina.Pregnancyoccursoncetheembryoattachestotheuterinelining.

AdvantagesofIVF:

- Highsuccessrateofpregnancy
- Addresses infertilityinbothmenandwomen
- Reducedriskofmiscarriage
- Availabletoanyone
- Use ofdonatedeggsorspermispossible
- Abilitytochoosetheoptimaltimingforpregnancy
- Increasedchancesofhavingahealthybaby

DisadvantagesofIVF:

- Riskofmultiplepregnancies
- Highcost
- Higher riskofanunsuccessfulcycle
- Possibilityofpremature birth
- Limitednumber ofeggsretrieved
- Potentialhealthissues
- Ethicalconsiderations

Fig. 1.4ProcedureofInVitroFertilization

1.5.2 IntrauterineInsemination(IUI)

Intrauterine insemination (IUI) is a fertility treatment commonly used when the male partner hasa low sperm count. The procedure involves collecting semen from the male partner and insertingitintothefemalepartner'suterus orvagina.Therearetwoprimarymethodsofartificialinsemination:intrauterineinsemination andintracervical insemination.In IUI, the semenisdirectlyintroducedintotheuterus,whileinintracervicalinsemination(ICI),thesemenis injectedintothecervix[39].

Advantages:

- NaturalcycleIUIcanbeperformed.

- Thespermwashing processenhancesspermquality.
- IUIislessinvasiveand morenatural.
- Thetreatmentdurationisshort.
- IUIis lessexpensivecomparedtootherfertilitytreatments.
- IUIincreasesthechancesofconceptioncomparedtoregularintercourse.

Disadvantages

- Highinterventionmaybenecessaryifcertainconditionsarenotmet:
    - Healthyandclearfallopiantubes.
    - Timingthepregnancytestwithovulation.
    - Adequatespermmotility.
- IUIhaslowersuccessratescomparedtotreatmentslikeIVF,withabouta20%successrate.
- Thereisahigherriskofmultiplepregnancies(twins,triplets,ormore)duetounpredictableeggfertilization.

1.5.3 ZygoteIntrafallopianTransfer(ZIFT)

Zygoteintrafallopiantransfer,alsoknownastubalembryotransfer,issimilartoinvitrofertilization (IVF). However, instead of placing the embryo in the uterus, it is transferred to thefallopiantube[32].

1.5.4 IntracytoplasmicSpermInjection(ICSI)

Intracytoplasmic sperm injection (ICSI) is often utilized by couples dealing with male infertility.It is also considered for older couples or those who have previously unsuccessful IVF treatments.Incontrasttoconventionalfertilization,wherespermandeggareplacedtogetherinapetridish toallownaturaltodiscussalternativeoptionsandthepossibilityofunsuccessfuloutcomesopenly.

Common treatments include hormonal therapy, surgery (to address endometriosis and fibroids),and assisted reproductive technologies such as artificial insemination and in vitro fertilization(IVF)[13].

CHAPTER-2

PLANTINTRODUCTION

Paederiafoetida,oftenreferredtoasskunkvineorstinkvine,isaspeciesofclimbingvinethatfallswithin the coffee family, Rubiaceae. This plant has established a significant presence acrossvariouswarmclimatezones,withaparticularconcentrationinthesouthernandsoutheasternpartsofAsia.Itsgeographicrangeencompassesbothtropicalandsubtropicalenvironments.Theplant'scommon names are derived from its most notable characteristic - a strong, unpleasant scent thatbecomesapparentwhenitsfoliageisdamagedorcrushed. Thisolfactoryfeaturehasplayedakeyrole in the plant's identification and nomenclature across different cultures and regions where it isfound[50].

2.1 COMMONNAMES

1. English:Chinesefevervine
2. Hindi(India):GandhaPrasarini
3. Bengali(BangladeshandpartsofIndia):Gandhabhaduli
4. Malayalam(Kerala,India):Talanili
5. Tamil(TamilNadu,IndiaandSriLanka): Mookuthi
6. Japanese:Hekusokazura
7. Chinese:JiShiTeng
8. Indonesian:Sembukan
9. Nepali:Birelahara
10. Assamese(Assam,India):Bhedailota

Fig. 2.1PaederiaFoetidaPlant

Fig. 2.2Paederiafoetidaflower

2.2 BOTANICALCHARACTERISTICS

Paederiafoetida exhibits distinctive botanical features that characterize its growth andappearance. This enduring, ligneous vine demonstrates remarkable climbing ability, oftenextendingtoimpressivelengthsmeasuringmultiplemeters.Itsfoliagearrangementisnoteworthy, withleavespositionedinpairsonoppositesidesofthestem. Theseleavesdisplayadistinctive lanceolate shape, tapering to a point. The plant's reproductive structures are equallynotable, featuring diminutive, cylindrical blossoms that typically manifest in hues ranging fromsoft pink to vibrant purple. As part of its life cycle, Paederiafoetida develops compact, globularfruits resembling berries. These fruits play a crucial role in the plant's dissemination strategy,housing seedsthatfacilitateitsspreadand establishmentinnewenvironments[31].

2.3 SCIENTIFICCLASSIFICATION

Table2.1: Taxonomyclassification

Kingdom	Plantae
Division	Magnoliophyta
Subdivision	Angiospermae
Class	Magnoliopsida

Order	Gentianales
Family	Rubiaceae
Tribe	Paederieae
Genus	Paederia
Species	PaederiafoetidaL.

2.4 ACTIVECOMPOUNDS

The medicinal benefits of Paederiafoetida are largely due to its diverse array of phytochemicals.Amongthese,sterolssuchasstigmasterolandβ-sitosterolplayasignificantrole. Additionally,theplant containsessentialfattyacids,including linoleicacid,andiridoidglycosides.Thesebioactivecompounds collectively contribute to the plant's potent anti-inflammatory, pain-relieving, andliver-protectingproperties[16].

2.5 ETHNOPHARMACOLOGY

Paederiafoetida has a rich history in traditional medicine across various cultures. Its leaves andotherpartshavebeenusedtoaddressawiderangeofailments. Infolkremedies,itwasemployedto treat rheumatism, urinary issues, and fevers. The plant's versatility extended to addressingdigestive problems, dental care, and arthritis. Its applications varied from topical use to internalconsumption,demonstratingitsperceivedtherapeutic potential.

The plant's medicinal properties are likely attributed to its diverse phytochemical composition.Scientific analysis has revealed that Paederiafoetida contains a variety of bioactive compounds,including polyphenols, flavonoids, tannins, and terpenoids. These components contribute to theplant's antioxidant capabilities, with substances like carotene and vitamin C playing significantroles. Theextract'sabilitytoneutralizefreeradicals,underscoresitsantioxidantpotential.

The health benefits of Paederiafoetida extend beyond its antioxidant properties. The phenoliccompounds present in the plant offer protection against organ damage and various diseases bycountering free radicals. Tannins, which are abundant in many plants including Paederiafoetida,havebeenassociatedwithantibacterialeffects.

Theseeffectsarethoughttoresultfromtheabilityof polyphenols and tannins to disrupt bacterial membranes, inhibit enzymatic activity, and formcomplexeswithmetalions.

Furthermore, the alkaloids found in Paederiafoetida contribute to its antimicrobial propertiesthrough their ability to interfere with the DNA and cell walls of pathogens. Studies have shownthattheplantexhibitsantibacterialactivityagainstbothgram-positiveandgram-negativebacteria.This broad-spectrum antimicrobial action is likely due to the synergistic effects

of its variousbioactivecompounds,includingpolyphenols,flavonoids,tannins,and alkaloids.

In essence, Paederiafoetida's traditional uses are supported by its rich phytochemical profile,which confers antioxidant and antimicrobial properties. These characteristics provide a scientificbasis for its long-standing use in folk medicine and suggest potential for further exploration inmoderntherapeuticapplications[45].

Fig. 2.3Paederiafoetidagrowinginwildcondition

Fig.2.4Paederiafoetidafruit

2.6 PHARMACOLOGICALACTIVITIES

1. HepatoprotectiveActivity:

The protective effects of a 70% ethanolic extract of Paederiafoetida leaves were assessed in a ratmodelfollowingparacetamoladministration.Subsequentinvitrotestswerecarriedouttoevaluatethe anti-hepatotoxic potential of the plant extract against hepatic lesions induced by paracetamol.The results showed significant increases in serum glutamate-pyruvate aminotransferase (SGPT),total protein, and serum glutamate-oxaloacetate transaminase (SGOT) levels at doses of 50, 200,and400mg/kgbodyweightoftheextract.Additionally,hepaticlipidperoxide(LPO)levelsinthepara cetamol-induced rats were significantly reduced by 40% with the plant extract. This suggeststhatPaederiafoetidamaybeusefulfortreatingvariousliverconditions,supportedbyotherstudie sindicatingamildhepatoprotective effect[24].

2. Anti-diarrhealActivity:

The 70% ethanolic extract of Paederiafoetida demonstrated anti-diarrheal effects in rats withdiarrhea induced by castor oil and magnesium sulfate. This effect was attributed to a significantextensionofthediarrheallatentperiodandareductioningastrointestinalmotility.Inthecastor oilexperiment,dosesof50,200,and400mg/kgresultedinadecreaseinthepurgingindex(PI)valuewithin one hour. At a dose of 500 mg/kg, the effect lasted for six hours. The plant extract alsosignificantly reduced the purging index value in a dose-dependent manner in diarrhea caused bymagnesiumsulfate.TheseresultsindicatethatPaederiafoetidahaspotentanti-diarrhealproperties[9].

3. Anti-diarrhealActivity:

The70%ethanolicextractofPaederiafoetidaexhibitedsignificantanti-diarrhealeffectsinrats

experiencing diarrhea induced by castor oil and magnesium sulfate. The observed effect was dueto a notable prolongation of the diarrheal onset period and a reduction in gastrointestinal motility.In the castor oil study, administering doses of 50, 200, and 400 mg/kg led to a reduction in thepurging index (PI) value within one hour. At a higher dose of 500 mg/kg, the effect persisted forsix hours. Additionally, the extract significantly lowered the purging index value in a dose-dependent manner in rats with magnesium sulfate-induced diarrhea. These findings suggest thatPaederiafoetidapossessesstronganti-diarrhealproperties[21].

4. AnalgesicActivity:

The analgesic potential was assessed in mice using the acetic acid-induced writhing inhibitionmethod.Atanoraldoseof150mg/kg,notableantinociceptiveactivitywasobserved.Theenzy meinhibitionwas21%byhexaneextract,9%byethylacetateextract,and19%bymethanolicextract.In

comparison, 50 mg/kg of aminopyrine reduced writhing by 63% in the same experiment. It isbelieved that the analgesiceffectstemsfromtheinhibitionofthe prostaglandinpathway[57].

5. AntibacterialActivity:

The antibacterial activity of Paederiafoetida extract was tested against Salmonella typhimurium,Escherichiacoli,andtwoGram-positivebacteria,StaphylococcusaureusandEnterococcusfaecalis. The extract showed antibacterial properties against S. flexneri, S. aureus, E. coli, and E.faecalis. Initial screening results indicated that S. flexneri was the most susceptible bacterium,while S. typhimurium was the least affected. The experiment confirmed that Paederiafoetidapossessesantibacterialproperties[26].

6. Anti-arthriticActivity:

Arthritisisachronicinflammatorydiseasethataffectsthejointsandsurroundingtissues.Paederiafoetida, a medicinal herb from South India traditionally used for rheumatoid arthritis, was foundto be more effective than Merremia tridentata. Furthermore, Paederiafoetida can reduce elevatedlevels of acute-phase proteins, offering a potential alternative to NSAIDs, which do not influencethese proteins[5].

7. AnticancerProperties:

Paederiafoetida is considered a disease-modifying anti-rheumatic drug (DMARD) with benefitsover nonsteroidal anti-inflammatory drugs (NSAIDs) due to its ability to lower elevated levels ofacute-phase proteins. Traditional medicine in Bangladesh suggests that the plant has anticancerproperties. This claim is supported by the demonstrated anticancer efficacy of a 50% ethanolicextractagainsthumannasopharyngealcarcinomaintissueculture.Theplant'santicanceractionislikelyduetoitsantioxidantoranti-inflammatoryproperties[20].

8. Anti-nociceptiveActivity:

Various pharmacological studies have validated the traditional medicinal use of Paederiafoetidaas a potent analgesic. Hexane and methanol extracts of Paederiafoetida exhibited strong anti-nociceptiveeffectsatadoseof300mg/kgbodyweightinSwissalbinomice,reducingaceticacid-induced writhing by 37.4%and 25%, respectively.Toinvestigate potential anti-nociceptivepathways,severalreceptorandionchannelblockerswereused,includingnaloxone,glibenclamide, nimodipine, and L-NAME. The results indicated that glibenclamide-sensitive K+-ATP channels were involved in the antinociceptive effects induced by Paederiafoetida, whilenimodipine-sensitive L-type Ca2+ channels were the primary mechanism through which thebutanol fraction (BF) prevented antinociception. The main components of Paederiafoetida, suchas sterols (stigmasterol and β-sitosterol) and fatty acids (linoleic acid), have been associated withanalgesic properties. The n-butanol fraction, rich in iridoid glycosides, was also investigated

foritsanalgesicqualities[28].

CHAPTER-3

LITERATURE SURVEY

1. **Ali B., *et al.*,2023:** The study assessed the prevalence of primary and secondary infertility in India by employing standard demographic definitions and analyzing data from four iterations of the National Family Health Survey (NFHS), conducted between 1992–1993 and 2015–2016. To identify significant changes in infertility rates over time, the t-test, Chi-square test, and bivariate analysis were utilized. A multivariate logistic regression model was applied to determine the extent of infertility among Indian couples from diverse socioeconomic backgrounds, lifestyles, and reproductive practices in 2015–2016. The findings revealed a consistent decline in primary infertility from 1992 to 2015, while secondary infertility increased from 19.5% in 1992–1993 to 28.6% in 2015–2016.

2. **Dutta P. P., *et al.*, 2023:** Paederiafoetida Linn., a widespread species in the Rubiaceae family, thrives across temperate and tropical Asian regions. This plant is notable for its distinctive characteristic: when its foliage or branches are damaged, they emit a potent, sulfur-like odor. For centuries, it has played a significant role in various traditional healing practices, including Chinese and Ayurvedic medicine, addressing a broad spectrum of health conditions. This article aims to provide a comprehensive overview of the plant's chemical composition and evaluate its potential applications in modern drug development.

3. **Dutta B., *et al.*, 2023:** This study aimed to evaluate the antioxidant and cholesterol-lowering effects of Paederiafoetida leaf extract. The researchers followed OECD 2006 guidelines for acute oral toxicity testing. They prepared the extract using an ethanol infusion method. To induce high cholesterol levels, rats were fed a high-fat diet consisting of coconut oil and vanaspati ghee (2:3 v/v) at 10 ml/kg body weight. The extract was administered at 500 mg/kg body weight. The study measured total cholesterol, triglycerides, HDL, and LDL cholesterol to assess the extract's ability to lower lipid levels. Antioxidant activity was evaluated by measuring malondialdehyde (MDA), catalase (CAT), and superoxide dismutase (SOD) using standard methods. This comprehensive approach allowed researchers to investigate both the lipid-lowering and antioxidant properties of P. foetida leaf extract, providing insights into its potential as a natural remedy for managing cholesterol levels and oxidative stress.

4. **Hyun J. Y., *et al.*, 2023:** Infertility poses a significant global health challenge, impacting not only physical well-being but also mental health, often manifesting as stress, depression, and fatigue. In recent years, there's been a growing interest in Traditional East Asian

Medicine (TEAM) approaches, particularly herbal prescriptions, as complementary treatments for women struggling with fertility issues.Despite this increasing attention, the scientific literature lacks comprehensive studies evaluating the efficacy of these herbal remedies for female infertility. Moreover, there's a noticeable gap in systematic analyses exploring the use of herbal medicines within the context of TEAM diagnostic patterns.

5. **Kambooj N., *et al.*, 2023:** To explore the individual and combined effects of daily habits, fertility journeys, and social background on mental health indicators - specifically tension, low mood, and worry - in both women who can and cannot conceive. The study also aimed to uncover how these psychological factors interact with each other across fertile and infertile groups.

6. **Malik N., *et al.*, 2023:** According to a 2020 WHO report, infertility affects 186 million individuals globally, with various factors contributing to both male and female reproductive challenges. Common culprits include stress, excessive alcohol consumption, smoking, and obesity. While conventional treatments and synthetic medications offer effective solutions, prolonged use often leads to unwelcome side effects such as weight fluctuations, headaches, mood swings, and hot flashes. In extreme cases, these treatments may even trigger depression and anxiety. Consequently, there has been a worldwide shift towards herbal remedies, with their popularity steadily increasing. This trend reflects a growing preference for more natural approaches to addressing infertility, potentially offering alternatives with fewer long-term adverse effects.

7. **Khamphaya T., *et al.*, 2022:** Paederiafoetida extract (PFE), derived from a plant native to Asia, is reputed for its potent antioxidant properties. This study aimed to investigate PFE's protective effects on the blood system, liver, and kidney functions in rats subjected to lead toxicity. The experiment involved six groups of male Wistar rats. One group received lead acetate (50 mg/kg body weight), another served as a control with 0.25% carboxymethylcellulose, and the remaining four groups were given lead acetate plus varying concentrations of PFE (50, 100, 500, or 1,000 mg/kg body weight). The treatment was administered daily to all rats for a period of eight weeks. Researchers monitored the animals' body weight weekly. The impact of lead acetate was evaluated through various measures, including body weight changes, hemoglobin levels, biochemical markers, and tissue examinations.

8. **Kotepui M., *et al.*, 2022:** Paederiafoetida, a plant indigenous to Asia, is purported to have strong antioxidant properties. Given this claim, our research sought to examine how extracts from this plant (PFE) might safeguard the hepatic, renal, and blood systems of rats exposed to lead toxicity.

9. **Sharma A., *et al.*, 2022:** The research aimed to investigate the psychological impact of inability to conceive on women experiencing primary infertility. Additionally, the study examined how various factors - including daily habits, reproductive health, and social

demographics - influenced mental well-being among North Indian women, both independently and through their complex interrelationships. The investigation encompassed 250 women diagnosed with primary infertility who sought care at a gynecology clinic, along with an equal number of age-matched fertile women from Delhi for comparison.

10. **Sharma R., *et al*., 2022:**Paederiafoetida Linn., native to subtropical regions, has been a staple in traditional medicine, addressing ailments from rheumatism to snake bites. Leaf analyses reveal a complex phytochemical profile, including volatile oils and flavonoids. To ensure consistency, researchers developed an HPTLC fingerprint of the hydroalcoholic leaf extractREF (HAPF). This investigation focused on assessing HAPF's subchronic toxicity, recognizing that repeated exposure effects are more relevant clinically than acute reactions. Following OECD protocols, scientists conducted an extended oral toxicity study on HAPF.

11. **Saha D., *et al*., 2022:** Paederiafoetida stands out as a plant widely utilized in both traditional and folk healing practices. Various parts of this herb have been employed locally for centuries as a natural treatment for a diverse range of health conditions. Research has revealed that Paederiafoetida possesses a remarkable array of therapeutic properties, including the ability to regulate blood sugar, improve lipid profiles, combat oxidative stress, protect kidney function, reduce inflammation, alleviate pain, suppress coughing, dissolve blood clots, heal ulcers, safeguard the liver, eliminate parasitic worms, and manage diarrhea. Furthermore, growing evidence suggests that several of its bioactive compounds also support sperm production, promote wound healing, address inflammatory disorders, and show promise in cancer treatment. These scientific investigations aim to uncover the underlying mechanisms responsible for these medicinal effects and identify potential targets for drug development.

12. **Walker M. H., et al., 2022:** Infertility is a distinctive condition that impacts not only the individual seeking treatment but also their partner, creating a shared experience of the diagnosis. While male infertility plays a crucial role in the overall discussion of reproductive challenges, this analysis focuses specifically on female infertility - its evaluation, management, and therapeutic approaches.

13. **Carson S. A., et al., 2021:** Infertility may be a symptom of an underlying chronic condition. Ovarian stimulation in IVF cycles typically involves clomiphene citrate, letrozole (an aromatase inhibitor), or gonadotropins. Gonadotropin use can lead to complications such as ovarian hyperstimulation syndrome (1-5% of cycles), causing fluid accumulation, electrolyte issues, and increased clotting risk. Multiple pregnancies are also a risk, occurring in up to 36% of cycles depending on the medication used. For patients with anovulation, ovulation induction with timed intercourse is often the initial approach. Couples dealing with endometriosis, mild male factor infertility, or unexplained infertility may try 3-4 cycles of ovarian stimulation before moving on to IVF if unsuccessful. This stepped approach balances the potential benefits of less invasive treatments with the need

for more advanced interventions when necessary, considering the specific factors contributing to each couple's fertility challenges.

14. **Goodarzi N., *et al.*, 2021:** The research results revealed that various parts of the studied plants contain high levels of beneficial compounds, particularly polyphenols like flavonoids and isoflavones, which play a crucial role in supporting female reproductive health. These plant-derived substances have been found to influence hormonal balance in women and provide relief from menopausal discomfort. Moreover, they show promise in addressing a range of reproductive disorders, including polycystic ovary syndrome (PCOS), premature ovarian failure (POF), endometriosis, excessive prolactin production, and hypothalamic issues. Beyond their reproductive benefits, these compounds exhibit cancer-fighting properties, combat oxidative stress, and help alleviate depression. Given their effectiveness and safety profile, these plant-based substances hold significant potential for use in both traditional healing practices and modern pharmaceutical development focused on women's health concerns.

15. **Rasheed H., *et al.*, 2021:** Furthermore, research suggests that the seeds of date fruits may enhance testicular defense against oxidative stress, improve blood chemistry markers, and boost testosterone production. This indicates that dates, including their seeds and extracted compounds, show promising therapeutic potential as a natural remedy for reproductive issues in both sexes. Studies highlight the diverse array of biologically active components and mechanisms through which Phoenix dactylifera and its various parts may exert beneficial effects on fertility.

16. **Roy P., *et al.*, 2021:** Over the past decade, herbal and Ayurvedic remedies have garnered global attention, impacting both medical practices and economies. This surge in popularity has sparked worldwide concerns about the quality, safety, and efficacy of herbal treatments. Among these plants, Paederiafoetida, a member of the Rubiaceae family, stands out for its diverse therapeutic applications. Traditional medicine systems employ this plant to address a wide array of health issues, ranging from liver disorders and rheumatoid arthritis to diabetes and respiratory conditions like asthma and coughs. It's also used for various digestive problems, including constipation, stomach pain, dysentery, and diarrhea. Additionally, P. foetida is believed to help with skin conditions, wounds, bone fractures, and even more serious ailments like typhoid, pneumonia, and cancer. This extensive list of traditional uses highlights the plant's potential significance in herbal medicine, while also underscoring the need for rigorous scientific evaluation of its properties.

17. **Sharma S. P., *et al.*, 2021:** Recent decades have seen significant progress in researching plant-based remedies for infertility and related conditions, yielding innovative and effective treatments. This study reviews Indian research on herbal medicines for female reproductive issues, analyzing 53 selected articles. The findings encompass 202 medicinal plants from 84 families, with 459 documented uses. The plant types include 62 trees, 55 shrubs, 79 herbs,

and 3 climbers. Roots and leaves are the most commonly used parts in medicinal preparations. The study identifies 84 plants for treating infertility, 79 for leucorrhea, 53 for menorrhagia, 29 for dysmenorrhea, 23 for amenorrhea, and 22 for other related disorders. This comprehensive overview highlights the rich diversity of plant-based treatments in traditional Indian medicine for addressing various female reproductive health issues, providing a valuable resource for further research and development in this field.

18. **Beiranvand R., *et al.*,2019:** Reproduction is a fundamental biological drive in humans. When individuals face difficulties conceiving, it can lead to a range of negative emotional experiences, collectively termed "well-being deterioration." This research aimed to examine the impact of infertility on women's overall life satisfaction. The findings revealed that while women struggling with fertility issues reported higher scores in social wellness compared to their fertile counterparts, they demonstrated significantly reduced ratings in other aspects of life quality, specifically mental well-being, physical health, and environmental contentment.

19. **Mazumder K.,*et al.*, 2018:** P. foetida's leaves and stems are utilized to create a juice, while its tender leaves are prepared as a dish with salt and chili. In Arunachal Pradesh, India, the Aka tribe, along with indigenous people from Bangladesh's Chittagong hill tracts, employ the leaf juice to address burns, dysentery, and diarrhea. Some Indian tribal communities reportedly consume the powdered whole plant to alleviate rheumatic pain and weakness.Despite its traditional use for diarrhea treatment, limited scientific investigation has been conducted on its mechanisms. This study aims to fill this knowledge gap by examining the anti-diarrheal action of P. foetida leaf extracts. Both aqueous and methanolic extracts are analyzed, combining a preliminary phytochemical screening with an exploration of their mode of action against diarrhea.

20. **Rooney K. L., *et al.*, 2018:** Infertility clearly causes stress, as infertile women often report elevated levels of anxiety and depression. However, whether stress contributes to infertility is less clear. Investigating the impact of distress on treatment outcomes is complicated by various factors, including inaccurate self-report measures and increased optimism at the beginning of treatment. Nonetheless, recent research indicates that psychological interventions can significantly alleviate psychological distress and are also associated with notably higher pregnancy rates.

21. **Shreffler K.M., et al., 2018:** Infertility is a vital topic for family scientists due to its impact on families, its relevance to related fields such as fertility trends and reproductive health, and its implications for professionals supporting individuals and couples facing infertility. In this review, we explore common myths about infertility awareness and treatment, and highlight new research involving men, couples, and untreated infertile individuals. Factors such as the significance of parenthood, experiences of childlessness, awareness of reproductive issues, and availability of resources are crucial for understanding treatment-

seeking behavior and psychosocial impacts. Drawing on findings from family science research, we provide specific recommendations for infertility practice within broader social contexts, including changes in healthcare, education, and employment.

22. **Zeng Y., *et al.*, 2018:** Polycystic ovarian syndrome (PCOS) is a common, multifaceted endocrine disorder affecting 5-10% of women of reproductive age. It is characterized by hyperandrogenemia, hirsutism, oligomenorrhea, amenorrhea, anovulation, numerous antral follicles, and hypersecretion of circulating LH with similar or lower levels of FSH. Research has shown that cinnamon can improve insulin sensitivity and enhance menstrual regularity in individuals with PCOS.

23. **Dubey S., *et al*., 2017:** Paederiafoetida Linn., a plant from the Rubiaceae family, is commonly used in traditional Indian medicine. It exhibits diverse therapeutic properties, including protecting against oxidative stress and liver damage, fighting parasites, managing blood sugar, relieving pain, reducing inflammation, and combating bacteria. This research aimed to investigate whether the alcohol-based extract of P. foetida and its key component, lupeol, could interfere with liver enzymes involved in the initial phase of drug processing. Various P. foetida extracts underwent qualitative analysis using advanced chromatography techniques. The impact of P. foetida extract on liver enzyme activity was assessed using two methods: the CYP450-carbon monoxide complex assay on rat liver microsomes, and a fluorescence-based test for specific enzyme subtypes (CYP3A4 and CYP2D6).

24. **Kashani L (M.D),*et al*., 2017:** Female infertility is a multifaceted issue that can involve either or both partners. The underlying factors contributing to infertility are not gender-specific: approximately 40% of cases are attributed to male-related issues, while about 50% stem from female disorders. It's noteworthy that in 25% of infertile couples, both partners experience fertility challenges.Herbal remedies are derived from a diverse array of natural sources, including various plant parts such as leaves, bark, flowers, roots, fruits, and berries. Evidence-based herbal medicine presents a promising avenue for addressing female infertility. This review aims to present compelling data supporting the efficacy of herbal treatments in managing female reproductive issues.

25. **Billah M. M., *et al*., 2015:** This research aimed to investigate the pain-relieving and neurological effects of leaf extracts prepared using water, ethanol, and ethyl acetate. The extracts were administered to mice at a dose of 400 mg/kg body weight. Pain-relieving properties were evaluated using two methods: the acetic acid-induced writhing test and the formalin-induced persistent pain test. The extracts' calming and anxiety-reducing effects were assessed using three behavioral tests on mice: the hole cross, open field, and elevated plus maze, all at the same dosage. Results showed that the ethanol-based extracts significantly reduced pain responses in both the formalin and acetic acid tests, while the other two extracts had a milder effect. In contrast, the water-based extract showed a moderate calming effect, whereas the other two extracts had minimal impact on sedation

and anxiety. The study notes that these specific leaf extracts have not been previously examined for these particular properties.

26. **Mohsen Nikseresht, *et al.*,2015:** Pomegranate juice is abundant in polyphenols such as punicalagin, ellagic acid, and gallic acid, as well as anthocyanins and vitamin C. The fruit has gained popularity for its ability to inhibit cell proliferation, induce apoptosis, block HIV-1 entry, and exhibit microbicidal, cardioprotective, and antihyperlipidemic properties. Pomegranates are known for their strong antioxidant capabilities and their effectiveness in scavenging free radicals. Dried pomegranate seeds contain amino acids like glutamic acid, as well as phytoestrogens such as genistein, daidzein, and coumestrol, and the estrogenic hormone estrone.

27. **Sharma V., *et al.*, 2014:** This study investigates plant-derived compounds, natural principles, and raw extracts that show promise in treating sexual disorders, enhancing sexual function, and supporting reproductive processes. The researchers conducted a comprehensive review of traditional Indian literature and scientific databases. They analyzed how current scientific findings align with traditional claims, offering insights into the rationale behind using plants as aphrodisiacs. The study presents a systematic categorization of active crude extracts and known phytochemicals, grouping them by chemical structure. It also provides information on their toxicity profiles, mechanisms of action, and pharmacological effects. By bridging traditional knowledge with modern scientific understanding, this research offers a valuable resource for further exploration of plant-based treatments for sexual and reproductive health. The comprehensive approach taken in this study lays a foundation for potential development of new, natural therapies in this field.

28. **Chanda S., *et al*., 2013:** Paederiafoetida has a long history of use in various cultures, both as a culinary ingredient and a therapeutic agent. Many of its health benefits are related to digestive health, suggesting its potential in addressing gastrointestinal issues. This comprehensive overview synthesizes information from diverse sources, exploring P. foetida's traditional uses, chemical composition, and medicinal properties. The plant shows particular promise in treating modern lifestyle-related conditions, especially stomach ulcers. Its efficacy underscores the importance of thoroughly evaluating plants used in indigenous medicine, and P. foetida may serve as a valuable resource in developing innovative pharmaceutical treatments.

29. **Devrorey P., *et al.*,2009:** The decision was made to increase the frequency of single embryo transfers (SETs) in ART cycles. It is expected that ongoing improvements in cryopreservation techniques, which enhance pregnancy rates by using surplus stored embryos, will boost the global adoption of SET. Fertility treatments can be tailored and adjusted for each patient to optimize safety and effectiveness. Personalized management plans and predictive models based on individual patient characteristics could represent

significant advancements in providing better care.

30. **Osman H., *et al.*, 2009:** Researchers evaluated the ability of Paederiafoetida and Syzygiumaqueum extracts, in both fresh and dried forms, to neutralize harmful free radicals. They employed two different testing methods: the ABTS assay, which uses a specific chemical compound to measure antioxidant strength, and the β-carotene bleaching technique. All extract samples demonstrated significant antioxidant properties, with effectiveness ranging from 58% to 80% across both tests. Notably, the fresh plant extracts outperformed their dried counterparts in terms of antioxidant potency for both species. The study also revealed a strong correlation ($R2 = 0.9849$) between the results obtained from the two different testing methods, suggesting consistency in the findings.

CHAPTER-4

AIM&OBJECTIVE

AIM:

TheobjectiveofthisstudyisInvestigationofPaederiaFoetidatowardsthefertilityinearlypostimplantation.

OBJECTIVE:

1. To improvethehighsuccessrateofpregnancy.
2. TostudyART techniquesusedtoimproveinfertilityproblems.
3. Theobjectivetoovercomeinfertilityratebyreducingstressandhormonalbalance.
4. Increasetheprobabilitythatmorehealthyeggsareproducedandreleased.

CHAPTER-5

PLANOF WORK

LiteratureSurvey

↓

CollectionandExtraction

↓

PreliminaryphytochemistryScreen

↓

IsolationofCompoundsbyColumn Chromatography

↓

CharacterizationofIsolatedpurecompoundbyMass,UV,IRandNMRSpectroscopy

↓

AssessmentofFertilityActivityofLeavesExtract

↓

In-VitroStudies

↓

Statisticalevaluation

↓

Submissionofthesis

CHAPTER– 6

MATERIALANDMETHOD

6.1 COLLECTIONOFPLANTEXTRACT

HiyaIndiaBiotechPvtLtd.,B-51,OkhlaIndustrialArea,Phase-1,NewDelhi–110020,providedthe paederiafoetidaextractthatwas purchased**.**

6.2 PRELIMINARYPHYTOCHEMICALSCREENING

By using phytochemical qualitative responses for common plant secondary metabolites, both P.foetida extracts were assessed. To identify steroids, alkaloids, coumarins, flavonoids, saponins,tannins,andphenolicacids,aphytochemicalscreeningwas carriedout.
The following chemicals and reagents were used for phytochemical screenings of the extracts:Libermann- Burchard reagent (for steroids), ferric chloride and potassium dichromate solutions(for tannins), saponins with the capacity to form stable foam, and Dragendroff's reagents (foralkaloids, mg, and HCl for flavonoids). Using the Carrez reagent, phenolic acid derivatives werefoundintheaqueousextractofP.foetidaleaves understudy[18].

6.2.1 Testforalkaloid

a. Mayer'sTest:

- Placeonemlofplantextractinatesttube.
- Fillthistest tubewith1mlofMayer'sreagent,potassiummercuriciodidesolution.
- Shakewelltoensurepropermixing.
- Watchthe precipitatesinthetesttubeastheydevelop.

Analysisofthe findings
Observetheformationofacreamywhiteprecipitate,which indicatethepresenceofalkaloids.

b. Wagnertest

The Wagner reagent is the term used to describe the iodine found in potassium iodidesolution. The Wagner reagent is also known as iodo-potassium iodide chemically. Thisreagent is made by dissolving 1 gram of iodine and 3 grams of potassium iodide in 50 mlofdistilledwater.For thistest,two to threemloftheplantextractarecombinedwithonemlofdilutedHCl

andafewdropsofWagner'sreagent.Thepresenceofalkaloidsisindicatedbytheformationofareddish-brownprecipitate.

6.2.2 Testforflavonoids

a. AlkalineReagentTest:

- Takeasmallamountoftheplantextractanddissolve itinasuitablesolvent(e.g.,ethanol,methanol,orwater).
- Addafewdropsof10%sodiumhydroxide(NaOH)orpotassiumhydroxide(KOH)solutiontothe extractsolution.
- Observe the formation of an intense yellow color, which becomes colorless upon additionofdilute hydrochloric acid (HCl),indicatingthepresence offlavonoids.

b. Lead AcetateTest:

- Takeasmallamountoftheplantextractanddissolveitinasuitablesolvent(e.g.,ethanol,methanol ,orwater).
- Addafewdropsof10% leadacetatesolutiontotheextractsolution.
- Observetheformationofayellow-coloredprecipitate,whichindicatesthepresenceofflavonoids.

6.2.3 TestforPhenols

- Theferricchloridetestinvolvesdissolvingatiny amountof theplantextractin anappropriate solvent,suchaswater,ethanol,ormethanol.
- Totheextractsolution,add afewdropsofa5%ferricchloride($FeCl_3$) solution.
- Watchforthedevelopmentof astrongblue,blue-black,orgreenhue,as thesearesignsthatphenolicchemicals arepresent.

b. TheLeadAcetateTest

- involvesdissolvingatinyamountofplantextractinanappropriatesolvent,suchaswater,ethanol, ormethanol.
- Totheextractsolution,add afewdropsofa10%leadacetatesolution.
- Watchforthedevelopmentofayelloworwhiteprecipitate,asthissuggeststhepresenceofphenolicchemicals.

6.2.4 TestforSteroid

a. Salkowskitest:

- Thistestaddsafewdropsofstrong sulfuricacid totheplantextractorsample
- Thepresenceofsteroidsisindicatedbythecreationofaredtintorareddish-brown ringattheinterfaceofthe twolayers.

b. Liebermann-Burchardtest:

In this test, concentrated sulfuric acid is gradually added down the test tube's side after theplantextractorsamplehasbeenmixedwithafewdropsofaceticanhydride. Thedevelopmentofabluish-greencolorshowsthepresenceofsteroid

6.2.5 Testforterpenoids

a. SalkowskiTest:

- To testforthepresenceofterpenoids,addafewdropsofstrongsulfuricacidtothe plantextractorsample.
- If areddish-brown colorationforms at theinterface,terpenoids arepresent.

b. Burchard-Liebermann

- Totestforterpenoids, mixtheplantextractorsamplewithafewdropsofaceticanhydride.
- Then, carefully pour concentrated sulfuric acid along the test tube's sides.
- Terpenoids willappearwhenablue-greentintappears.

6.2.6 Test forAminoacids

a. NinhydrinTest:

- Combineasmallamountofplantextractwithasolutionoftheninhydrinreagent.
- Gentlywarmthemixture.
- Thedevelopmentofapurpleorblue-purplehuesignifiestheaminoacidcontent.

b. Biurettest:

- Addafewdropsofcoppersulfatesolutionandsodiumhydroxidesolutiontotheplantextract
- If avioletorpinkhueappears,itindicatesthepresenceof aminoacidswithtwoormorepeptidebonds.

6.2.7 SaponinTest

a.FoamTest:
The alcoholic extract was given a forceful shaking with distilled water. When stable foam beginstoform,saponinis present.

6.3 EXPERIMENTALANIMAL

The study used Female and Male Albino Rats weighing 140-160 gm and aged 6-12 weeks. TheratswerehousedinourInnovativeCollegeofPharmacy'sprimaryanimalfacilityinGreaterNoida,India.Theywerehousedintheanimalhomeunderstandardlaboratorysettings.Ratswerehousedin polyacrylic cages with a maximum of five animals per cage, air conditioning, and natural lightand dark cycles, at a temperature of 25°C (± 2°C) and relative humidity of 50% - 70%. The studyprotocol met the standards of the Committee for the Control and Supervision of ExperimentsAnimals and was approved by the institutional animal ethics committee's (IAEC) guidelines forthe managementanduseofresearchanimalsinexperiments[52].

6.4 METHODOFADMINISTRATION

The oral gavage needle was secured in place by the 1 ml tuberculin syringe. This was used in thedrug suspension administration process. With one hand, the gavage needle was grasped while theothercarefullyrestrainedthemousebythescruffoftheneck.Thealbinorats'esophagusandmouthwere gently punctured with a gavage needle. After then, the plunger was gradually depressed toinjectthemedicationsuspensionortestmaterialstraightintothestomach.Usingthesamegavageneedle ,0.1–
0.2mlofdistilledwaterweregivenfollowingthetestmaterialtoguaranteefulldosageadministration.
Care and technique were used to prevent the rat from suffering an esophagealinjuryorreceivingmedicationbyaccidentthroughthetrachea[3].

6.5 PHARMACOLOGICALSCREENINGTECHNIQUESTOEVALUATEFERTILITYACTIVITY

6.5.1 ESTROUSCYCLE

The reproductive cycle in rodents is known as the estrous cycle. It is analogous to the menstrualcycle, which refers to the ovarian and uterine cycles that make up the human reproductive cycle.The four stages of the four- to five-day estrous cycle are proestrus, estrus, metestrus, and diestrus[4]. On the 26th day following birth, mice enter the estrous cycle and reproductive period whenthevaginaopens.Thishappensapproximatelyten daysbeforevaginalcornification[38].

The aim of the estrous cycle monitoring in the control and SRE treated females was to ascertainthe impact of Piper betides' secondary root extract on the cyclicity pattern and exfoliated vaginalcytology.SixnumbersofadultcyclicfemalesineachgroupofcontrolandSREtreatmenthasbeenconsidered for study of estrous cycle.The cell types during different phases of estrous cycle werestudiedfollowingthemethodofMontesandLuque(1988).Briefly,thevaginalfluidwascollectedregularly in the morning hour (7.00 – 9.00 hrs) with the help of a smooth dropper filled withdistilled water. Approximately 0.5ml distilled water was taken either in a micro tip or a smalldropper and flushed the vaginal fluid 2 to 3 times. The collected fluid was spreaded on a cleanslide to prepare a smear and allowed for air dry. Dried slides were gently placed in methanol for2-3 minutes and again left for air dry. Following the methanol treatment, the slides were put inGiemsa stain for 5 minutes for staining cells of vaginal smear and then it was observed under thelightmicroscope.
Thecycle isdivided into fourcharacteristicphases:proestrus,estrus,metestrusanddiestrus.Proestrus:

- Identifiesthedaybeforetheovulation
- Takesabout12 hours.
- The preponderance of tiny nucleated epithelial cells that are not cornified. These cellsmightshowupsinglyor ingroups.Theremayoccasionallybesomecornifiedcellsinthesample.

Estrus:

- Atthisphase, ovulationtakesplace
- Endsinup to12hours.
- Clustersofbig, cornifiedsquamousepithelialcellsareseen.
- Thecytoplasmisgranular,theformisuneven,andthereisnodiscerniblenucleus.

Metestrus:

- Around21 hoursinduration
- Avarietyofcelltypesarepresentatthisstage,withleukocytes(neutrophils)predominating and a small number of nucleated epithelium and/or cornified squamousepithelialcells.

Diestrus:

- Requires48–72hourstocomplete.
- Leukocytes, or neutrophils, predominate in this stage, with a small number of nucleatednon-cornifiedepithelialcells.

6.5.2 Varioustechniquesforvaginalcytology

Numerous research works have presented different approaches to assess the estrous cycle byconsideringthealterationsinthephysiologyandanatomyoftheanimal.Thesetechniquesincludevisu al evaluation, vaginal cytology, histological study of the reproductive organs,vaginal wallimpedance ,urinebiochemistry,andvisualassessment.
Comparabletotheocularevaluation,vaginalcytologyisalso commonlyused.It appearsto bethemethod most frequently employed to ascertain the estrous cycle's phases. It is reasonably pricedand non-invasive. This procedure is accurate and dependable for microscopic analysis of thevaginal discharge cells, despite the fact that it does demand some level of ability. But it has alsobeennotedthatthis approachislaboriousandtime-consuming[48].

Gathering a sampleofvaginalcytologyusing wetsmear:

- Holdtheanimaldownorraiseitup byitstailbase.
- Usegauzemoistenedwithsalinetocleanthevulvaandensurethatnosecretionsareblockingits entry.
- Foreveryanimal,use a freshpipetteorpipettetip.
- Put20–100µLofPBS orsalineintoapipetteformiceand 40–200 µLforrats.
- Formiceandrats,insertthеplasticpipettetiptoadepthofroughly1-2 mmand5-10mm,respectively.
- It is important to be cautious when inserting the tip to prevent cervical stimulation.Overstimulating oneself may result in pseudopregnancy, which manifests as a persistentdiestrusthatlasts forupto14days.
- UsethesamePBS/salinesolutiontogentlyflushthevaginathreetofivetimes.
- Fillthepipettetipwiththelastflush.
- Enough material will be produced for vaginal cytology observation in a volume of 10 µLofsolution.
- Applyasmallcoatingoffluidtoafreshlycleanedmicroscopeslide.

Evaluationofthesample

- Smearscanbeexamined wetandunstainedveryawayafter collection,ortheycanbelefttoairdryatroomtemperature.
- Afterfixingorairdrying,slidescanalsobestainedwithametachromaticormultichromatic stain.

- Lookattheentiresmearsincevariouspartsoftheslidemayhavedifferent cellkindsandcounts.
- Usea10×objectivetoexaminesmearsunderamicroscope.Uselowlightlevelsinthemicroscop eto see thecells;donot usethecondenserlenstoprovidegoodcontrast.
- The40×objectivelensfacilitatessimplerbutthepercentageofeachofthethreecelltypesdetermi nesthe estrouscyclephase,andusing the 10× objectivemakesthis
- simplertodiscern.

6.6 COLLECTIONOFBLOOD

Using surgical forceps and scissors, each adult rat was given a chloroform vapor anesthesia in adesiccator before being dissected. Using a sterile syringe and needle, blood samples were drawnintoplainsampletubesviacardiacpuncture.Thesampleswerethenlefttoclotfor120minutesatroo m temperature. The serum was then extracted by centrifuging the samples for 10 minutes at3000rpmusingabenchtopUniscopeLaboratoryCentrifuge.Theseraacquiredfromthecorresponding Pasteurpipetteswereusedtocarefullyremovetheappropriatesamplesintoplasticspecimen bottles that were labeled appropriately. The samples were then frozen in a bio-freezeruntil they were ready for analysis. For histological investigations, ovarian and uterine sampleswerepreservedin10%formalsalineinplainbottleswithlabels.Thetissueswereprocessedusingt hetypicalroutinehistologytechniques as outlinedbyBrownUsing. A light microscope to examine the slides, histological alterations were noted and recordedatX40magnification,distinguishingbetweennormaland deterioratedtissue[23]

6.7 HORMONEASSAY

Diagnostic Automation, provided the prolactin, progesterone, estradiol, follicle-stimulating, andluteinizing hormone assay kits. Glass-distilled water was utilized to prepare all other analyticalgrade chemicals in a volumetric flask. The method outlined in the hormone assay kits was usedforallhormonalanalyses,i.e.,prolactin,estradiol,progesteroneluteinizing,andfollicle-stimulatinghormones,inaccordance withtheprinciple[17].

6.8 FERTILITYACTIVITY

Estrogenic Activity in Immature Female Rats Immature female rats of Wister strain 21-23 daysoldandweighing40-
60gwereused.Theywereseparatedintosixgroupsofsixanimalseach.Theselectedgroups weretreatedasfollows:
GroupI:control(salinesolution)
GroupII:referencestandard(Clomiphene0.02mg/kg)
Group III; ethanolic leaves extract of paederiafoetida (100 mg/kg)GroupIV:ethanolicleavesextractofpaederiafoetida(300mg/k

g)

Group V: aqueous leaves extract of paederiafoetida (1000 mg/kg)GroupVI;aqueousleavesextractofJatrophagossypifolia(300mg/kg)

Thetreatmentwasgivenforsixdays,24hafterthelasttreatment;alltheanimalsweresurrenderedby decapitation, and uteri were dismembered out, cleared off the adhesive tissue, stained on filterpaper,andweighedspeedilyonasensitivebalance(MartinandFinn,1970).Thetissueswerefixedin Bouin's fixative for 24 h. dehydrated in alcohol, and entrenched in paraffin blocks werepartitioned at 6 \i and stained with hematoxylin eosin solution (H and E Stain) for histologicalobservations[54].

Table6.1ExperimentalGroup

S.No	Group	Animals	Mating	Treatment	Dose
		Malealbinorat-3	Yes		
I	Control group	Female albinorat-6	No	Vehicle	
II	Negative group	Female albinorat-6	Yes	Sertraline	20mg/kg
III	Standard drug	Female albinorat-6	Yes	Clomiphene	20mg/kg
IV	TestGroup-1 (PFEX)	Femalealbinorat-6	Yes	Paederiafoetida Ethanolic Extract	100mg/kg
V	TestGroup-2 (PFEX)	Femalealbinorat-6	Yes	Paederiafoetida Ethanolic Extract	300mg/kg
VI	TestGroup-3 (PFAX)	Femalealbinorat-6	Yes	Paederiafoetida AqueousExtract	100mg/kg
VII	TestGroup-4 (PFAX)	Femalealbinorat-6	Yes	Paederiafoetida AqueousExtract	300mg/kg

CHAPTER-7

RESULT

7.1 PRELIMINARYPHYTOCHEMICALSCREENING

7.1.1 AssayforAlkaloid

a. Mayer'sAssay:

● Acreamywhiteprecipitatewasobserved.

b. Wagner'sAssay:

● Areddish-brownprecipitatewasobserved.

7.1.2 AssayforFlavonoids

a.AlkalineReagent Assay:

● Anintenseyellowcolorappeared, whichturnedcolorlessuponaddingdilutehydrochloric acid(HCl).

7.1.3 LeadAcetateAssay:

● Ayellowprecipitateformed.

7.1.4 AssayforGlycoside

a. Keller-KillianiAssay(AssayforDeoxySugars):

● Areddish-brownringformedat theinterfaceofthetwolayers.

b. Borntrager'sAssay(AssayforAnthraquinoneGlycosides):

● Apinkcolordevelopedintheammonia layer.

7.1.5 Assay forPhenol

a. FerricChlorideAssay:

● Anintensebluecolorappeared.

b. Lead AcetateAssay:

● Awhiteprecipitateformed.

7.1.6 AssayforSteroid

a. SalkowskiAssay:

● Noreddish-brownringappearedattheinterfaceofthetwolayers.

b. Liebermann-BurchardAssay:

● Nobluish-greencolorwasobserved.

7.1.7 Assay forTannins

a. FerricChlorideAssay:

● Nobluish-greencolorwasobserved.

b. Lead AcetateAssay:

● Ayellowprecipitateformed.

7.1.8 AssayforTerpenoids

a. SalkowskiAssay:

● Areddish-browncolorationappearedattheinterface.

b. Liebermann-BurchardAssay:

● Ablue-greencolor developed.

7.1.9 AssayforAmino Acid

a. NinhydrinAssay:

● Abluish-purplecolorappeared.

b. BiuretAssay:

● Apurplecolorwasobserved.

7.1.10 Assay forSaponin

a. FoamAssay:

● Stablefoamdidnotform.writethisdatainthe

7.2 Determinationofthresholddose:Effectsestrouscycle

- Paederiafoetidadosesadministered:100mg/kg,300mg/kg,and1000mg/kgbodyweight/day
- 300mg/kg/dayidentifiedasthresholddose
- Vaginalcytologyexaminedfor 16days(fourconsecutiveestruscycles)
- Implantationsites countedonday6ofgestation

7.2.1 EffectsofthresholddoseofPaederiafoetidaextractonvaginalcytologyCont

rolrats

Regularestrouscyclewithlargenumbersofcellsinsmears

Paederiafoetidatreatedrats

The study observed a notable reduction in exfoliated cellsin vaginal smearsfollowing theadministrationofPaederiafoetida.Thesechangesbecameapparentfromthefifthdayoftreatment.Specifically,therewasasignificantdecreaseinbothkaryopyknoticandcornifiedcellsduringtheproestrusandestrus phases ofthe estrous cycle.

Quantitative analysis revealed a marked decrease in the number of karyopyknotic cells during theproestrus phase, with control group counts averaging 243.62 ± 5.24 compared to 95.50 ± 3.63 inthe Paederiafoetida-treated group. Similarly, the number of cornified cells in the proestrus phasealsodecreased,withcontrolgroupcountsat58.75±3.79versus22.37±2.21inthetreatedgroup.During the estrus phase, a reduction in karyopyknotic cells was also observed, with control groupcounts averaging 47.88 ± 2.22 compared to 21.23 ± 0.59 in the treated group. The number ofcornifiedcellsintheestrusphaseshowedasignificantdecreaseaswell,withcontrolgroupcountsat269.13±4.19versus104.13±3.88inthePaederiafoetida-treatedgroup.

Interestingly, despite these reductions in specific cell types, the overall rate of maturation fromkaryopyknotic to cornified cells remained unchanged. This suggests that while Paederiafoetidaeffectivelyreducesthetotalnumberofcertaincelltypes,it doesnot alterthefundamentalprocessofcellmaturation.

7.2.2 EffectofaThresholdDoseofPaederiafoetidaonimplantation

The study examined the effects of varying doses of Paederiafoetida on implantation sites andpregnancy rates in treated subjects. The control group had an average of 7.5 ± 0.18 implantationsites. At a dosage of 100 mg/kg/day, there was no significant effect observed, with the averagenumberofimplantationsitesbeing6.8±0.22,similartothe control.

However, increasing the dosage to 300 mg/kg/day resulted in a statistically significant reductioninthenumberofimplantationsites,withanaverageof3.5±0.26sites.Thehighest dosagetested,1000 mg/kg/day,led toa further significantreduction, with an average of only 0.5 ± 0.18implantationsites.

The pregnancy rates were also affected by the dosage of Paederiafoetida. Both the control groupand the 100 mg/kg/day group maintained a 100% pregnancy rate, indicating no adverse effects atthisdosagelevel. However, at300mg/kg/day, thepregnancyratedroppedto50%,indicatingthatgestationwas suppressedin50%ofthefemales treatedatthis dosage.

The most pronounced effect was observed at the highest dosage of 1000 mg/kg/day, where thepregnancy rate plummeted to 12.5%, meaning that gestation was suppressed in 87.5% of thefemales. This significant reduction highlights the strong impact of Paederiafoetida at high dosesonreproductiveoutcomes.

7.3 EffectsofPaederiafoetidaextractonovarianfollicle

Thestudyexaminedtheeffectsof Paederiafoetidaonovarianfolliclesinfemalerats.Inthecontrolgroup, the ovaries exhibited normal follicular development, characterized by the presence ofmultiple follicles at various stages of growth and numerous corpora lutea. The Graafian follicles,in particular, were well-developed and showed typical structural organization. In contrast, ratstreated with Paederiafoetida extract at a dose of 300 mg/day for 16 days displayed significantalterationsintheirovarianmorphology.Thetreatedovariesshowedsignsoffolliculardegeneration, with a noticeable reduction in the number of preantral follicles. The oocytes withinthese follicles appeared to be deteriorating, surrounded by disorganized granulosa cells that hadlosttheirnormalarrangementandfunction.TheGraafianfollicles,whicharecrucialforovulation,were themostseverelyimpacted.Thesefollicles exhibitedapronouncedloss of structuralintegrity, with granulosa cells becoming detached from the follicle wall and showing signs ofdegeneration. Healthy oocytes were scarce in these follicles, indicating a potential impact onfertility.Moreover,thenucleioftheremaininggranulosacellsappearedpyknotic,asignofcellulardeath or degeneration. These observations suggest that Paederiafoetida treatment significantlydisrupts normal ovarian function and follicular development, potentially affecting reproductivecapacityinfemalerats.

7.4 EffectsofPaederiafoetidaonhistologicalstructuresofuterus

Thestudyexaminedtheeffectsof Paederiafoetidaontheuterinelining(endometrium)comparedtoacontrolgroup.Thecontrolgroupshowedanormalhealthyuteruswithasmoothsurfacelining(luminal epithelium) consisting of columnar cells. The underlying stromal tissue, which providessupport and structure, was compact and contained glands. In contrast, the uteri treated withPaederiafoetida displayed several abnormalities. The lining became thin with a sparse layer ofepithelial cells. Endometrial hyperplasia, a thickening of the lining, was observed in some areas.These hyperplastic regions contained multinucleated cells, indicating abnormal cell division. Theepithelial cells also showed signs of damage, with pyknotic nuclei (dense and shrunken) andfragmentation. The glands within the lining had a thin epithelium with desquamation, suggestinga shedding of cells. Interestingly, the nuclei within the glandular epithelium and hyperplasticregionsexhibitedstrongbasophilicstaining,apossibleindicationofincreasedproteinproduction.Finally,thesupportivestromaltissuebecame looseandcontainedvacuoles,whicharesmallfluid-filledcavities.

In simpler terms, this study suggests that Paederiafoetida treatment may disrupt the normalstructure and function of the uterine lining. This is concerning as a healthy endometrium isessential for implantation and a successful pregnancy. More research is needed to determine thelong-termeffects ofPaederiafoetida onthe uterusandits overallsafety.

Incontrolgroupitwasobserved

- Smoothendometrialluminalepitheliumwithcolumnarcells
- Compactendometrialstromaltissuewithglands

IntestGroup

- Tithdesquamation
- Strongbasophilicstaininginnucleiofglandularepitheliumandhyperplasicregions
- Loosestromaltissuewithvacuoleformationofthinluminalepithelialcelllining
- Endometrialhyperplasia insomeareas
- Multinucleatedcellularstructuresinproliferatedareas
- Pyknoticandfragmentednucleiinepithelialcells

7.4.1 Effectsofextractofon uterinehistology during day 2 today6 ofgestation

ThePaederiafoetidaextracthasbeenadministeredtothefemaleratsduringtheperiimplantation.Oral administration has been carried out from day 1 to day 6 of gestation, while the histologicalstudy of the uterus has been carried out from day 2 to day 6 of pregnancy. The pregnancy wasdeterminedbythepresenceofspermsonthevaginalsmearsasmentionedelsewhere.Theobjectiveof the study was to determine the effects of the Paederiafoetida on uterine histology during thisearlystageofgestation.
Asmentionedearlier,eachday(fromday2today6ofgestation),onesetPaederiafoetida treated pregnant female along the vehicle treated control have been sacrificed tostudythe effectofPaederiafoetida (ifany)onuterusduringthe periimplantationperiod.

7.4.2 Uterinehistology on day2ofgestation

The results of the study of uterine histology on day 2 of gestation in both vehicle treated controlandPaederiafoetidaadministeredfemaleshasbeenpresented.
Theresultsshowedthatthenormalpregnant females possess the uterus with closure lumen and wellarranged epithelial cells in theuterine endometrial surface epithelium. The day 2 pregnant control rat's uterus showed welldeveloped rounded endometrial gland (eg) attached with the stromal (s) tissue as shown in thefigure. The cells of luminal epithelium are arranged uniformly and smoothly in the endometrialluminal surface. Administration of Paederiafoetida to pregnant females showed thin luminalepithelial(le)celllliningontheendometrialsurfaceepithelium.Theuterinelumenappearedmore wide than that of the respective control. The endometrial glands (eg) have been elongated andirregular
inshape.Theglandularepitheliumhasbeenobservedtobedesquamatedfromsupportingstroma following Paederiafoetida administration (Fig.15 B1). The Paederiafoetida treated day 2pregnant uterus showed cellular mitosis at certain places with accumulation of nuclei in theepithelial lining which is deeply stained by H & E staining. The area of deeply stained cells hasbeen appeared to be the characteristic of endometrial hyperplasia (eh) as presented in Fig.15B2.4.6.2

7.4.3 Uterinehistology on day 3ofgestation

The results of the study of uterine histology on day 3 of gestation in both vehicle treated controland Paederiafoetida administered females has been presented in. The results of the control day
3pregnantrat'suteruspossessedproliferatedendometrialluminalepitheliumwithsmoothlyarranged luminal epithelial (le) cells The luminal epithelial cells exhibited columnar appearance,while the lumen appeared narrow on day 3 of gestation. The multinucleated structures indicatedthe proliferation of the uterine luminal epithelium as presented B2. The endometrial glands havebeenfoundtoberoundedandsmallerinsizeembeddedintheuterinecompactstromaregion.Theoral administration of PaederiafoetidaPaederiafoetida to pregnant females at the dose of 500mg/kg/day affects the uterine tissue on day 3 of gestation (Fig.16 B, B1&B2). The uterine lumen(ul) remains wide with lesser degree of proliferation of luminal epithelium (le) in comparison tothat of the control. It has been observed that the uterine luminal epithelium exhibited signs ofdesquamation (dese) at certain places from the stromal tissues. At the same time, the luminalepitheliumshowedtheproliferationoftheluminalepithelialcellswithappearanceofmultinucleated structures.A number of endometrial glands have been observed in the Paederiafoetida treated female's uterus on day 3 of gestation. These glands have been observed to besmallerandlocatedinthedeeperregionofendometrialstroma.

7.4.4 Uterinehistology on day 4ofgestation

The histological structures of day 4 pregnant rats' uteri following treatment of vehicle (control)and 500mg/day Paederiafoetida has been presented. The results showed that the control pregnantfemales possess the uterus with narrow lumen and wellarranged epithelial cells in the uterineendometrial surface epithelium. The uterine luminal epithelium appeared with single nucleatedepithelialcellswithoutanysignoffurtherproliferation.Anumberofendometrialglandswithwelldevelopedglandularepitheliumhavebeenobservedinthestromaltissueofthecontrolrat'suteruson day 4 of gestation. In addition, proliferation of blood vessels in the stromal tissue has beenfoundtobecharacteristic oftheuterusonday4ofgestation.

Administration of Paederiafoetidafrom day1 onward of gestation in the threshold dose asmentioned elsewhere abrogated the structural organization of the uterine luminal epithelium onday 4of gestation.Theuterinelumenremainswidewithlesserdegree of proliferationofendometrial glands The luminal epithelium showed endometrial hyperplasia with cellular mitosisatmultipleareasofthelumen.Thisstructurallyaberrantluminalepitheliumhasbeendesquamated fromthestromaltissueofthePaederiafoetidaextracttreatedrat'suterus.Moreover,theseaberrantcellular structures showed strong eosinophilic staining properties as presented. Lesser number ofendometrial glands has been appeared in the uterine stroma following Paederiafoetida treatmentfromday1ofgestationonward.Inaddition,absencebloodvesselsproliferationinthestromal

tissue has been speculated to be the result of adverse effect of oral administration of secondaryrootextractofPiperbetle sides.

7.4.5 Uterinehistology on day 5ofgestation

The results of the study of uterine histology on day 5 of gestation in both vehicle treated controlandPaederiafoetidaadministeredfemaleshasbeenpresentedThecontrolfemale'suterusshowe duniformly arranged luminal epithelial cells in the endometrial surface epithelium. The epithelialcellsappearedsinglenucleatedandattachedtothecompactstromalzone.Theendometrialglan dshave been observed with well defined glandular epithelium. The proliferating blood vessels havebeen found in the stroma of the uterus on day 5 of gestation in control females. Administration ofPaederiafoetida to the pregnant females showed abrupt changes in the luminal epithelial (le) celllining on the endometrial surface epithelium on day 5 of gestation . The uterine tissue on day 5 ofgestationofPaederiafoetidatreatedfemalesexhibitedproliferatedluminalepitheliumandcomparativ ely thinner stromal zone. Vacuoles appeared in the luminal epithelial cells indicatingcellulardegeneration.Anumberofendometrialglandshavebeenfoundembeddedinthestrom a.Theluminalepithelialcellsappearedmultinucleatedatthebasalregionofthecolumnarepithelialcellsa ndwerehighlyeosinophilic.Althoughanumberofendometrialglandshaveappearedintheuterusonday5 ofgestation, manyoftheseglandswerefounddegeneratedaspresentedinthe.Thestromal cells just below the endometrial surface epithelium showed formation of vacuoles in thePaederiafoetidatreatedrat'suterusonday5ofpregnancy.

7.4.6 Uterinehistology on day 6ofgestation

Theresultsofthestudyofuterinehistologyonday6ofgestationinvehicletreatedcontrolfemaleshavebee npresented.

The day6 of gestation in rodents has been considered as the post implantation period and ischaracterized by appearance of decidual cell (dc) in the implantation sites., formation of theprimary decidual zone in control rat' uteri indicated the embryo implantation. The uterus showedendometriallumenwithsmoothlyarrangedluminalepithelial(le)cells.Thenumberofendometri alglands has been observed to be decreased in the stromal tissue on day 6 of gestation. The oraladministration of Paederiafoetida to the pregnant females at 500 mg/kg/day induced structuralaberrationofthenormalday6uterinehistology.AbsenceofdecidualizationinthePaederiafoeti datreated rat's uterus on day 6 of gestation suggested the effects of secondary root extract of Piperbetleoidesinthestromalcellsoftheuterus.It hasbeenobservedthatthestromalcellsonday6ofgestation following Paederiafoetida administration failed to form the primary decidual zoneleading to the failure of embryo implantation. The endometrial luminal epithelium has beenobserved to be desquamated (dese) from the basal stromal tissue. Few endometrial glands withdegenerating structures were observed in the stromal region following Paederiafoetida treatmentintheuterus

onday6ofgestation.Withthedesquamationofendometrialsurfaceepithelium,the

stromal tissue of the Paederiafoetida treated females on day 6 of gestation has appeared loose instructure.

7.5 DeterminationofSerumHormones

The findings showed that the FSH levels of the female immature rats administered with N. sativaextractdidnotexhibitsignificantdifferencescomparedtothecontrolgroup.Conversely,theserum LH level demonstrated a statistically significant increase ($p < 0.05$) in the N. sativa-treated groupin comparison to the control and standard groups (Figure 7B). Similarly, the serum P4 levelsshowed statistically significant elevations ($p < 0.001$) in both the N. sativa-treated and standardLHgroupscomparedtothecontrolgroup.Furthermore,theserumE2levelsexhibitedstatisticall ysignificant increases ($p < 0.0001$) in both the N. sativa-treated and standard E2 groups relative tothecontrolgroup.

a table based on the uterine histology from day 2 to day 6 of gestation, comparing control andPaederiafoetida-treatedrats

Table 7.1 Based on the uterine histology from day 2 to day 6 of gestation, comparingcontrolandPaederiafoetida-treatedrats

Day of Gestation	**Control**	**PaederiafoetidaExtract**
Day2	Closeduterinelumen,Well-arrangedepithelialcells,Rounded endometrialglands,Uniformands moothluminalepithelium	Wide uterine lumen, Thin luminal epithelialcelllining,Elongatedandirregularen dometrial glands, Desquamated glandularepithelium,Endometrialhyperplasi a(characteristiccellularmitosis)
Day3	Narrowuterinelumen,Proliferati ve endometrial luminalepithelium,Columnarlu minalepithelialcells,Rounded,s mallerendometrialglands	Wide uterine lumen, Less proliferation ofluminalepithelium,Desquamationoflumin alepithelium,Smallerendometrialglandsinde eperstroma,Appearanceofmultinucleatedstr ucturesinluminalepithelium

Day4	Narrowuterinelumen,Well-arrangedsinglenucleatedepithelial cells, Well-developedendometrial glands, Proliferation of blood vessels instroma	Wideuterinelumen,Endometrialhyperplasia (characteristic cellular mitosis),Desquamationofluminalepithelium, Fewerendometrialglands,Absenceofbloodvesselproliferation
Day5	Uniformlyarrangedluminalepithelial cells, Single nucleatedepithelialcells,Well-definedendometrial glands, Proliferatingbloodvesselsinstroma	Abruptchangesinluminalepithelium,Thinner stromal zone, Vacuoles in luminalepithelialcellsindicatingdegeneration,Degeneratedendometrialglands
Day6	Appearanceofdecidualcells,Formation of primary decidualzone,Smoothluminalepithelium,Decreasednumberofendometrialglands	Absenceofdecidualization,Failureofprimary decidualzoneformation,Desquamatedluminalepithelium,Fewdegeneratingendometrialglands,Loosestromaltissuestructure

Table7.2 Comparisonofcontroland Paederiafoetida ondifferent celltypesand phases

CellType	Phase	Control	Paederiafoetida
Karyopyknotic	Proestrus	243.62± 5.24	95.50± 3.63
Cornified	Proestrus	58.75± 3.79	22.37± 2.21
Karyopyknotic	Estrus	47.88± 2.22	21.23± 0.59
Cornified	Estrus	269.13± 4.19	104.13± 3.88

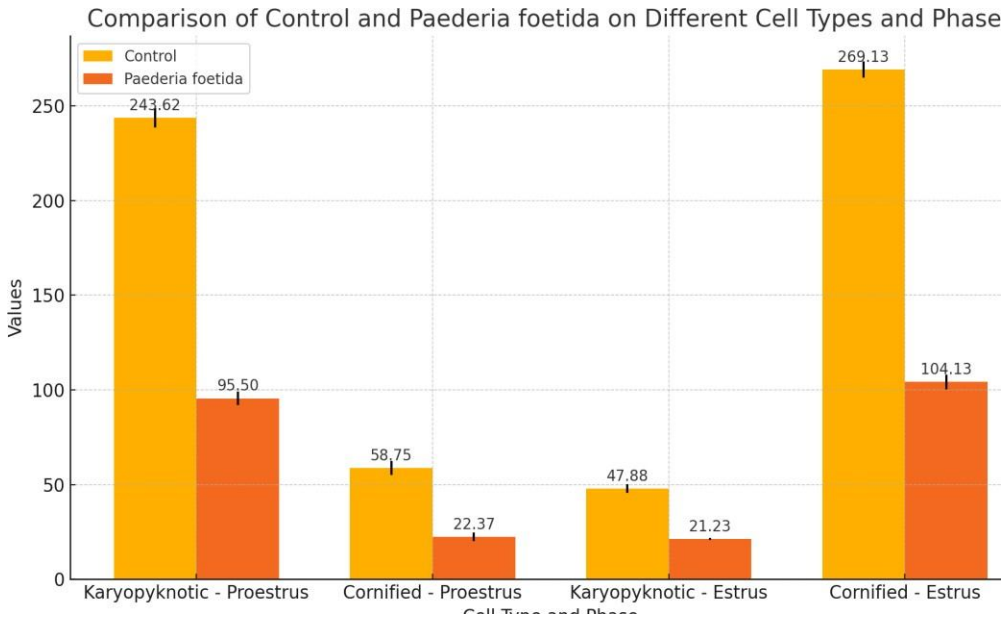

Fig.7.1Comparison ofcontrolandPaederiafoetidaondifferentcelltypesandphases

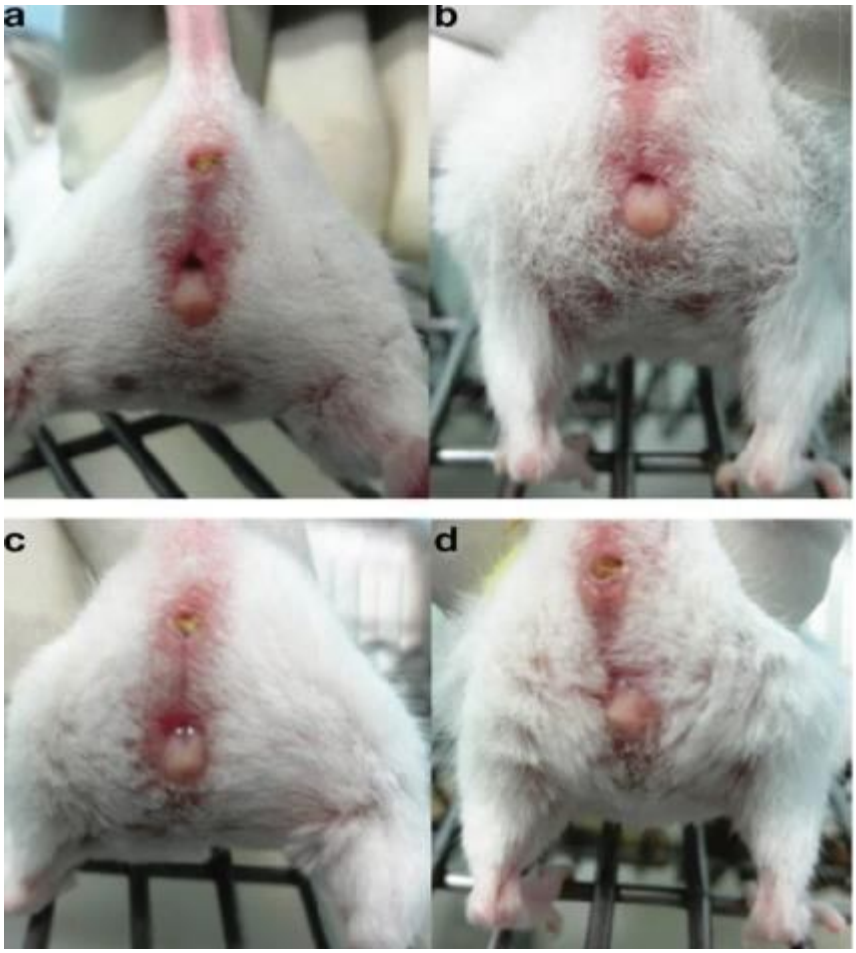

Fig.7.2Changesincellatdifferentstagesa-Proestrus, b-Estrus, c-Metestrus, d-DiestrusTable7.3Pregnancyrate, implantationsitesofdifferent groups

Group	**ImplantationSites**	**PregnancyRate**
Control	7.5± 0.18	100%
100mg/day	6.8± 0.22	100%
300mg/day	3.5 ± 0.26 (statisticallysignificant)	50% (suppressed gestation in 50%females)
100mg/day	0.5± 0.18	12.5%(suppressedgestationin87.5%females)

Table7.4ChangeswhentreatedwithPaederiafoetidagroupvsnormal

Aspect	**Control**	**Paederiafoetidatreated(300mg/dayfor16days)**
FollicularDevelopment	Normal	Normal
Degeneration	-	Fewerpreantralfollicles;MostaffectedGraafianFollicles
FollicleCount	Multiple follicles	Notspecified
CorporaLutea	Present	-
GraafianFollicles	Well-developed	Loss of structural organization; Detached anddegeneratinggranulosacells
OocyteCondition	Normal	Degenerated;Lossofhealthyoocytes
GranulosaCells	Normal	Disorganized;DetachedanddegeneratinginGraafianfollicles
StructuralOrganization	Normal	Lossofstructuralorganization inGraafianfollicles
Granulosa Cell Status	Normal	PyknoticnucleiinGraafianfollicles
OocyteHealth	Healthy	-

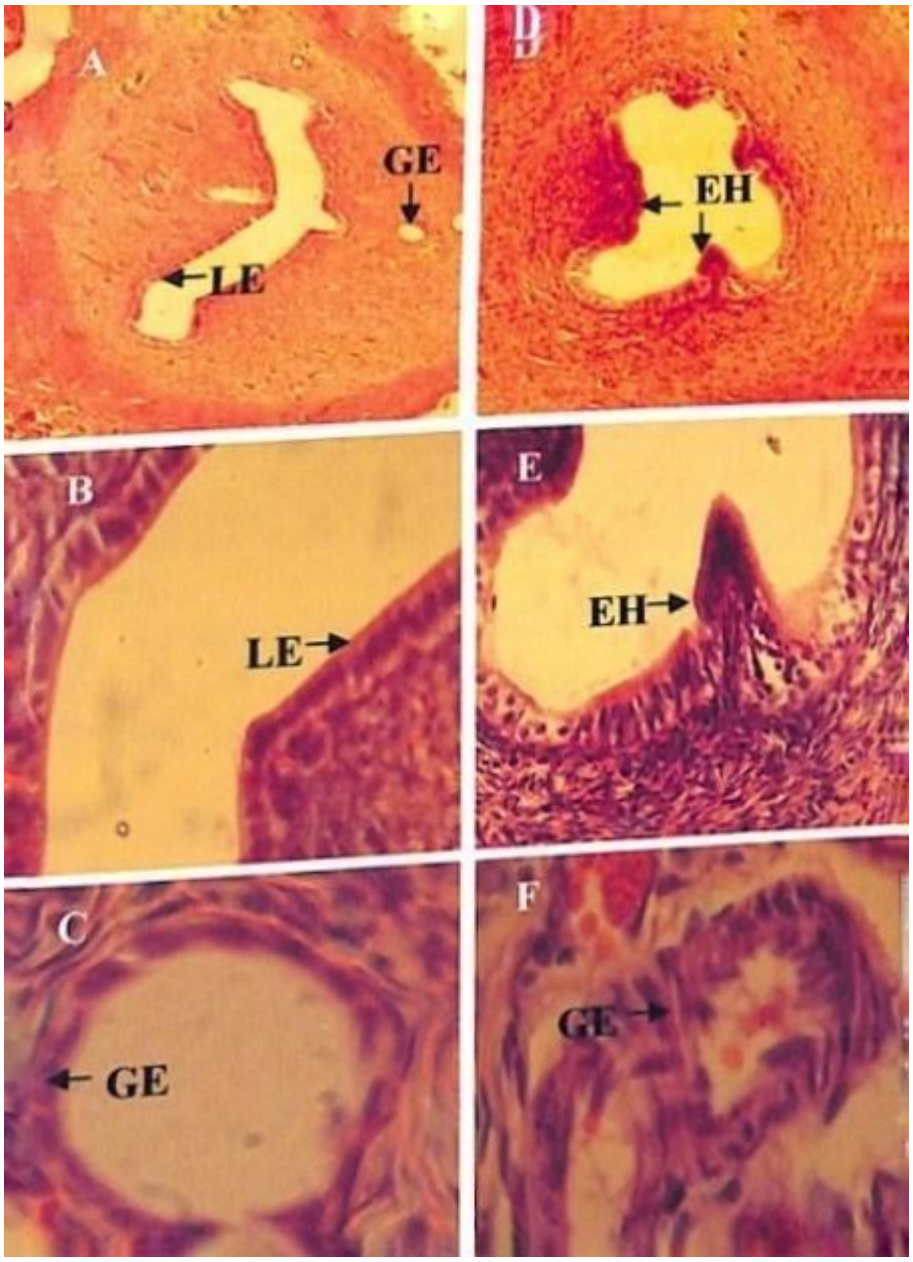

Fig.7.3Photomicrographsofuterinesectionendometrium Paederiafoetidatreatedfemaleshowing luminalepithelium, endometrialhyperplasia glandularepithelium

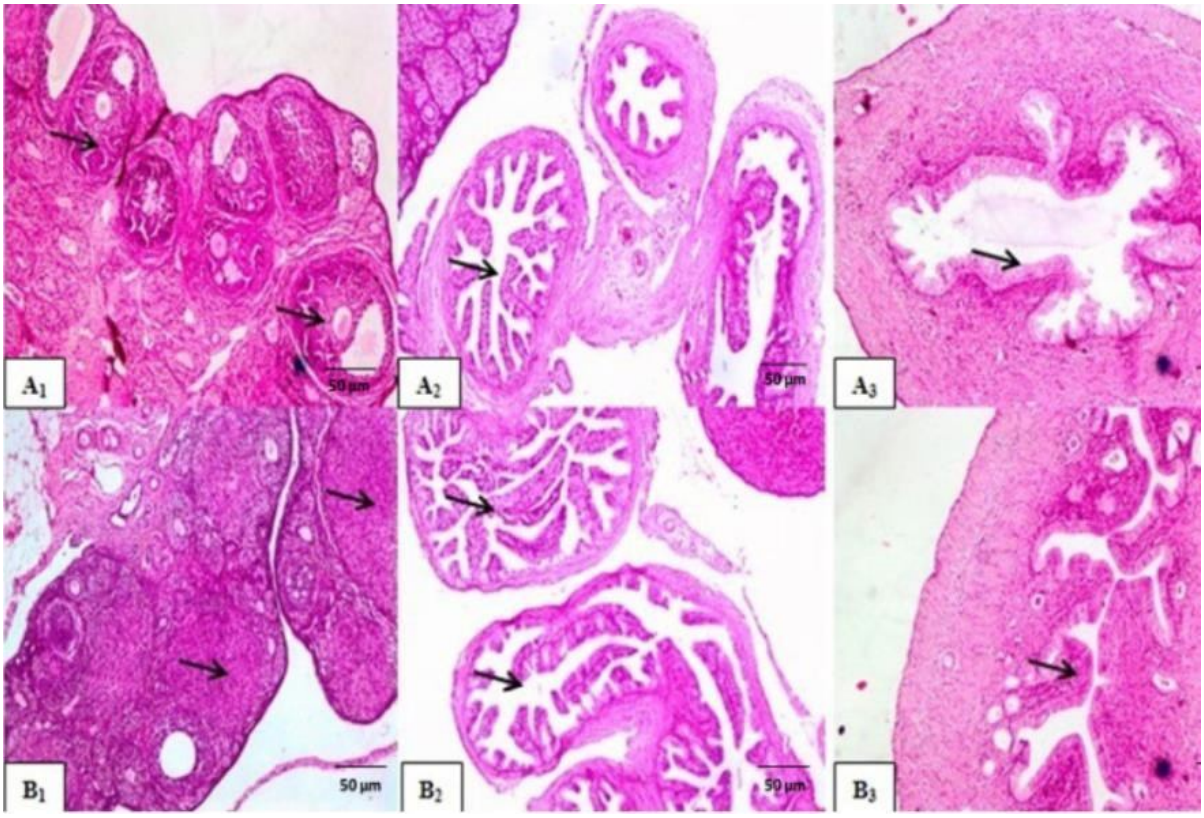

Fig7.4CSofovarian,

Follicularstimulatinghormonemimicactivityofextract*Paederiafoetida*identifiedbytheseeingofmultipleactive follicles

CHAPTER-8

DISCUSSION

Thiscomprehensivedissertationexaminesthecomplexlandscapeoffemaleinfertility,apervasiveglobal healthissueaffectingcountlessindividuals.Theresearchdelvesintothemyriadfactorscontributingtoinf ertilityinthemodernera,includingheightenedstresslevels,increasedexposureto environmental radiation, and the prevalence of processed foods lacking in essential nutrients.Thestudyemphasizesthatinfertility, definedastheinabilitytoconceiveormaintainapregnancytofullterm,extendsfarbeyonditsphysicalman ifestations.Itprofoundlyimpactsemotionalwell-being and often carries a significant social stigma, leading many to suffer in silence. This societalreticencesurroundingfertilityissuescompoundstheemotionalburdenexperiencedbythoseaffe cted.

At its core, female fertility hinges on the intricate dance of hormones within the hypothalamic-pituitary-ovarian axis. Any disruption to this delicate balance can compromise ovulation and,consequently, fertility.Theresearchalsohighlightshowphysicalconditionssuchasendometriosisorpelvicinfectionsc ancreateobstaclesinthereproductivetract,furthercomplicatingconceptionefforts.Moreover,thestudy underscorestheinevitabledeclineinovarianfunctionandspontaneouspregnancyratesthataccompanie s advancingage.

A significant portion of the thesis is dedicated to an in-depth exploration of two medicinal plants:Paederiafoetida and Paederia scandens. These plants, long utilized in traditional medicine forvarious ailments, are examined for their potential applications in fertility treatment. The researchpresents a detailed analysis of their phytochemical profiles, which include compounds such asiridoids,flavonoids,and aromaticoils,suggesting possibletherapeuticbenefits.

The dissertation also provides a comprehensive overview of contemporary fertility treatments. Itexamines procedures such as Intrauterine Insemination (IUI), where specially prepared sperm areintroduced directly into the uterus to enhance conception chances. The study elaborates on moreadvanced techniques like In Vitro Fertilization (IVF), where eggs are fertilized outside the bodybeforebeingimplantedintheuterus.Additionally,itdiscussesvariationslikeZygoteIntrafallopian Transfer(ZIFT),wherefertilizedeggsareplacedin thefallopian tubes,andIntracytoplasmic Sperm Injection (ICSI), a specialized form of IVF used in cases of severe maleinfertility.

A key strength of this research lies in its holistic approach. It not only explores the biological andmedical aspects of infertility but also acknowledges the profound psychological impact of thecondition. The thesis highlights how the emotional distress associated with infertility is oftenintensifiedbysocietaltaboosthatdiscourage opendiscussionoftheseissues.

By bridgingtraditionalherbalknowledgewith cutting-edgereproductivetechnologies,thisstudy

offers a multifaceted perspective on infertility treatment. It advocates for an integrative approachthatcombinesthewisdomoftraditionalmedicinewiththeprecisionofmodernscientificmetho ds.In conclusion, this thesis makes a significant contribution to both the scientific understanding ofpotentialherbaltreatmentsforinfertilityandthebroaderdiscourseoncomprehensivefertilitycare.It emphasizes the need for a compassionate, patient-centered approach that addresses both thephysical and emotional aspects of infertility. By exploring diverse treatmentmodalities andhighlightingtheimportanceofdestigmatizingfertilityissues,thisresearchpavesthewayformoreinc lusiveandeffectivestrategies inaddressingthecomplexchallengesoffemaleinfertility.

CHAPTER-9

CONCLUSION

Thiscomprehensivedissertation presentsan in-depth exploration of themultifacetedissuessurrounding female infertility, with a particular focus on North Indian women. The researchencompassesawiderangeoffactors,frompsychologicalwell-beingtotraditionalherbalremedies,providingaholistic viewofthis complexhealthconcern.

The study's foundation rests on a meticulous analysis of 250 women diagnosed with primaryinfertility in Delhi, compared against an equal number of fertile women of similar ages. Thiscomparative approach offers valuable insights into the intricate relationships between lifestylehabits, reproductive health, and socio-demographic factors. The research illuminates how theseelementscollectivelyshapethementalhealth landscapefor womengrappling withinfertility.

A key finding of the thesis is the profound emotional and psychological toll that infertility exactson women. It meticulously examines the intersection of societal expectations, cultural pressures,and individual health circumstances, revealing how these forces coalesce to impact mental well-being. This aspect of the study underscores the often-overlooked psychological dimensions ofinfertility,highlightingthe needforcomprehensive support systems.

The dissertation also ventures into the realm of traditional medicine, focusing on PaederiafoetidaLinn.,aplantindigenoustosubtropicalclimates.Thisplanthasarichhistoryinfolk medicine fortreatingvariousailments.Theresearchbreaksnewgroundbydevelopingahigh-performancethin-layerchromatography(HPTLC)fingerprintoftheplant'shydroalcoholicleafextract.Furthermore,it conducts rigorous subchronic toxicity assessments, providing crucial data on the plant's safetyprofile and potential therapeutic applications. This scientific approach to traditional remediesbridgesthe gapbetweenancientwisdomandmodernmedicalstandards.

In its exploration of female infertility, the thesis provides a comprehensive overview of currentevaluation methods, management strategies, and therapeutic interventions. It carefully weighs therisksand benefits associated with variousfertility treatments,including ovarian stimulationtechniquesandinvitrofertilization(IVF).Thisbalancedanalysisoffersvaluableinsightsfor bothmedicalprofessionalsand patientsnavigating thecomplexlandscapeoffertilitytreatments.

A significant portion of the research is dedicated to investigating plant-derived substances andtheir potential role in supporting female reproductive health. This aspect of the study not onlyhonorstraditionalknowledgebutalsopointstowardsfuturedirectionsinpharmaceuticaldevelopment. By examining how these natural compounds might be integrated into modernmedicalapproaches,the thesisopensupnew avenuesforholisticfertilitytreatments.

Thestrengthofthisdissertationliesinitsmultidisciplinaryapproach.Itseamlesslyintegrates

medicalscience,psychology,andtraditionalherbalmedicinetoprovideacomprehensiveunderstanding of female infertility. This holistic perspective acknowledges the complexity of theissue, recognizing that effective solutions must address not only the physiological aspects ofinfertilitybutalsoits psychologicalandsocialdimensions.

In conclusion, this thesis makes a significant contribution to the field of reproductive health. Itoffers a nuanced understanding of the challenges faced by women with infertility, particularly intheNorthIndiancontext.Bycombiningrigorousscientificanalysiswithsensitivitytoculturalandpsychological factors, the research provides a robust foundation for developing more effective,patient-centeredapproachestoinfertilitytreatment.Theintegrationoftraditionalherbalknowledge with modern medical practices suggests promising directions for future research andtreatmentmodalities,potentiallybenefitingcountlesswomenstrugglingwithinfertilityworldwide.

CHAPTER-10

SUMMARY

This extensive dissertation offers a thorough examination of female infertility, encompassing itsetiology, societal impact, and potential therapeutic approaches. The research underscores thepervasivenatureofinfertility,affectingasignificantglobalpopulation,andattributesitsprevalenceto contemporaryfactorsincludingheightenedstresslevels,increasedradiationexposure,dietarychanges, genetic factors,evolvinglifestyles,andtheubiquityofelectromagneticfields.

A key aspect of the study is its recognition of the profound emotional toll of infertility, oftenexacerbatedbysocietalstigmathatdiscouragesopendialogue.Thethesisdelvesintothephysiologi calunderpinningsoffemalefertility,emphasizingthecriticalroleofthehypothalamic-pituitary-ovarian axis in maintaining reproductive health. It elucidates how disruptions in thisdelicatehormonalbalancecanleadtoovulatorydysfunction.Additionally,theresearchhighlightsho w physical conditions such as endometriosis or pelvic infections can compromise fertility byaffecting the fallopian tubes. The study also addresses the impact of aging on fertility, noting thedeclineinovarianfunctionandspontaneousconceptionratesovertime.

A significant portion of the dissertation is dedicated to exploring the medicinal properties ofPaederiafoetidaandPaederiascandens.Theseplants,withtheirrichtraditionaluses,areexaminedfor their potential in addressing various health issues, including infertility. The thesis presents adetailedanalysisoftheirphytochemicalcomposition,highlightingthepresenceofcompoundslikeirido ids,flavonoids,andvolatileoils,whichsuggestpromisingtherapeuticapplications.Particularattention is given to Paederiafoetida's historical use in treating gastrointestinal disorders and itspotentialinaddressinglifestyle-relatedconditionssuchas gastric ulcers.

The research also provides a comprehensive overview of diagnostic techniques employed infertility assessments.Theseincludeadvancedimagingmethodslikesonohysterography andtransvaginalultrasonography,aswellasmoreinvasiveproceduressuchasendometrialbiopsyandlap aroscopy.Thethesisdiscussestheroleofassistedreproductivetechnologies(ART)ininfertilitytreatmen t, emphasizing the importance of tailoring management strategies to individual patientprofiles.

A key strength of this study lies in its integrative approach, bridging the gap between traditionalherbalknowledgeandmodernscientificmethodologies. Byexploringthepotentialofplant-basedtreatments in addressing sexual and reproductive health issues, the research opens new avenuesfor developing natural therapies. This holistic perspective not only honors traditional wisdom butalsoalignswithcontemporarytrendstowardsmorenaturalandpersonalizedmedicalinterventions.

In conclusion, this thesis makes a significant contribution to the field of reproductive health byoffering a multifaceted view of female infertility. It combines rigorous scientific analysis with anappreciationfortraditionalmedicinalpractices,providingacomprehensiveresourceforresearchers, healthcareprofessionals,andindividualsseekingtounderstandandaddressinfertility.The study's emphasis on developing personalized treatment approaches and exploring naturalremediesreflectsaforward-thinkingapproach toreproductivehealth,potentially benefitingcountlessindividualsstrugglingwithinfertilityworldwide.

CHAPTER-11

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CERTIFICATE

Certified that **REENA SHARMA** (**Enrollment No.** 2202270986005) has carried out the research work presented in this thesis entitled "**INVESTIGATION OF PAEDERIA FOETIDA TOWARDS THE FERTILITY IN EARLY POST IMPLANTATION**" for the award of **Master of Pharmacy** from Dr. APJ Abdul Kalam Technical University, Lucknow under my supervision. The thesis embodies results of original work, and studies are carried out by the student herself and the contents of the thesis do not form the basis for the award of any other degree to the candidate or to anybody else from this or any other University/Institution.

Signature

Dr. Amarjeet Singh

(Principal)

Innovative College of Pharmacy

Greater Noida

Innovative College of Pharmacy
Plot No. 6, Knowledge Park-2,
Greater Noida

PRINCIPAL

Signature

Mrs. Renu Tiwari

Assistant Professor

Innovative College of Pharmacy

Greater Noida

Date: