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Reproductive Effects of Medicinal Plants from the Zagros Mountains: A Systematic Review

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A B S T R A C T

Objective: Infertility is a global challenge affecting couples and can arise from various factors. Oxidative stress has been implicated in reproductive dysfunction, highlighting the protective role of antioxidants. Certain medicinal plants with antioxidant properties have traditionally been used to support reproductive health. This review focuses on the effects of *Pistacia atlantica*, *Capparis spinosa*, *Matricaria chamomilla* L., and *Ferulago angulata* plants commonly found in Iran's Zagros Mountains on the reproductive system. We systematically reviewed studies examining the effects of these Zagros-native plant species on infertility, analyzing findings from multiple scientific databases using qualitative methods.

Methods: A comprehensive search was conducted in Persian and English databases, including PubMed, Scopus, ScienceDirect, Google Scholar, SID, and Magiran, covering publications from 2000 to December 2024. The search terms included ("Fertility" OR "Reproductive System" OR "Testis" OR "Oocyte" OR "Sexual hormone" OR "LH" OR "FSH" OR "Testosterone" OR "Semen") AND ("Zagros Mountains" OR "*Pistacia atlantica*" OR "Baneh" OR "*Matricaria chamomilla*" OR "Chamomile" OR "*Capparis spinosa* L" OR "Caper" OR "Legji" OR "*Ferulago angulata*" OR "Chavir"). From an initial 342 screened articles, 51 were deemed relevant, and 17 fully matched the inclusion criteria and were analyzed.

Results: Most studies reviewed reported positive effects of these plants on infertility-related parameters, including improved gamete quality and reproductive hormone regulation. A limited number of studies noted adverse effects at specific dosages.

Conclusion: Extracts of *Pistacia atlantica*, *Capparis spinosa*, *Matricaria chamomilla* L., and *Ferulago angulata* may improve fertility by promoting healthy gamete production. Careful elimination of unnecessary or toxic compounds, adherence to appropriate dosages, and optimization of extraction methods are essential to maximize therapeutic benefits and minimize side effects.

Keywords: Pistacia, Capparis, Matricaria, Ferulago, Antioxidants; Infertility, Oxidative Stress

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Introduction

Infertility has emerged as a major global health concern affecting a substantial proportion of couples [1]. Evidence indicates that oxidative stress plays a pivotal role in reproductive dysfunction by increasing free radical levels in the reproductive system [2]. Specifically, oxidative stress arises from an imbalance between reactive oxygen species (ROS) and antioxidant defenses, which can significantly impair male fertility. While ROS are normal by-products of cellular

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metabolism, excessive accumulation triggered by toxins, infections, or environmental stressors can damage reproductive cells and compromise function [3]. For instance, elevated ROS levels contribute to varicocele development, a key factor in male infertility [4].

In women, oxidative stress is closely associated with polycystic ovary syndrome (PCOS), contributing to hallmark features such as insulin resistance, hyperandrogenism, and chronic inflammation. PCOS patients frequently exhibit abnormal oxidative stress markers, reflecting impaired antioxidant defenses, mitochondrial damage, and increased cell apoptosis. Moreover, mitochondrial tRNA mutations have been linked to metabolic complications in PCOS, including diabetes and hypertension [5]. ROS exert destructive effects through mechanisms such as protein oxidation, mitochondrial dysfunction, and lipid peroxidation, accompanied by elevated oxidative markers like malondialdehyde (MDA) and catalase (CAT) [6–8]. Antioxidant molecules—including glutathione (GPx), superoxide dismutase (SOD), vitamins, and natural plant compounds can neutralize ROS-induced cellular damage [9–11].

Excessive ROS in males induces apoptosis in sperm cells, leading to reduced sperm count and quality [12]. Additionally, ROS-mediated lipid peroxidation compromises plasma membrane integrity and fluidity, impairing motility and fertilization capability due to mitochondrial dysfunction [13–16]. In females, high ROS concentrations negatively affect oocyte maturation, particularly in immature oocytes prone to cell cycle arrest [17]. Consequences include increased granulosa cell apoptosis, antral follicle atresia, impaired steroidogenesis, and dysregulation of reproductive hormones such as luteinizing hormone (LH) and follicle-stimulating hormone (FSH) [18].

Previous studies have suggested that medicinal plants with antioxidant and therapeutic properties may mitigate oxidative stress and reduce free radical-induced damage [19]. The Zagros vegetation zone, covering the western half of Iran and extending into southeastern Turkey and Iraq (Figure 1), hosts a diverse range of plant species with potential reproductive benefits [20].

Pistacia atlantica, locally known as baneh and belonging to the pistachio family, has traditionally been used to treat bacterial and viral infections, inflammation, and gastrointestinal disorders [21]. Its high phenolic content confers potent antioxidant properties that protect against free radical-induced damage [22].

Matricaria chamomilla L. (chamomile), a member of the Asteraceae family, contains triterpenoids, phenolic compounds, coumarins, and flavonoids, which contribute to its therapeutic effects [23–25]. Research has explored chamomile's efficacy in diabetes [26], neurological disorders [27], metabolic dysfunction [29], and reproductive system modulation [28,30].

Capparis spinosa L., locally known as legji or caper, is a perennial plant traditionally used in various therapeutic contexts [31–33]. It contains phenols, triterpenoids, flavonoids, and other bioactive compounds with notable antioxidant properties [34–39]. Studies indicate its potential as an anti-diabetic and anti-hypertriglyceridemic agent [40]. This review examines its effects on reproductive health.

Ferulago angulata, known as chavir and a member of the Apiaceae family, has traditionally been employed for antimicrobial, anti-diabetic, reproductive-enhancing, and anti-hemorrhoidal purposes [41–45]. Its essential oil contains approximately 49 compounds with antioxidant and antibacterial activities [46–48]. This review assesses its role in fertility and reproductive system function, as summarized in Tables 1–2.

The present study systematically investigates the effects of selected Zagros-native plants on infertility. Relevant literature was retrieved from multiple scientific databases and analyzed qualitatively to provide a comprehensive overview of their potential reproductive benefits.

Materials and Methods

Search strategy

This systematic review followed Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines (http://prisma-statement.org/prismastatement/Checklist.aspx). In this regard, an extensive electronic search was undertaken on November 2024, in the Web of Science, EMBASE, PubMed, Scopus, SID, and MAGIRAN databases. The following search terms were used to perform the search All the indexed searches were limited to Persian and English with the terms ((“Fertility” OR “Reproductive System” OR “Testis," "Oocyte" OR "Sexual hormone" OR "LH" OR "FSH" OR "Testosterone" OR "Semen,")AND("Zagros mountains" OR " Pistacia atlantica," OR " Baneh," OR“ Matricaria chamomilla " OR "Chamomile" OR “Capparis spinosa L “ OR ”Caper” OR ”Legji” OR "Ferulago angulata” OR “Chavir”)) from 2000 to 29 December 2024. Their medical subject headings (MeSH) equivalents, combined with operators (AND, OR) and searched in databases.

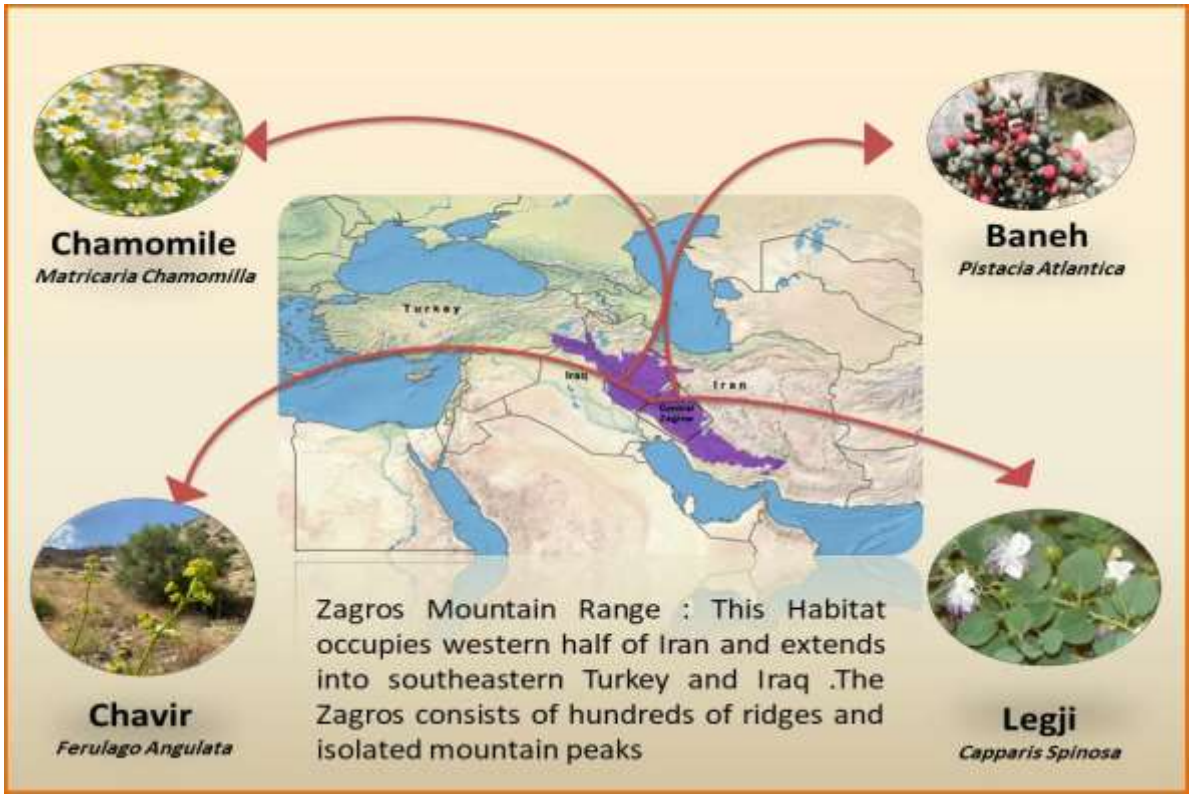


Figure1: Medicinal plants with antioxidant properties native to the Zagros Mountains [49–51].

Study selection

All references retrieved from the aforementioned databases were imported into EndNote X8 (Thomson Reuters, 8 November 2016), and duplicate records were removed. Two researchers independently screened titles and abstracts to identify potentially relevant studies. Based on predefined inclusion criteria, in vitro and in vivo studies investigating the effects of the selected plants on infertility were included in this systematic review. Studies without accessible full texts were excluded. Subsequently, the full texts of all eligible studies were independently reviewed by the investigators. The study selection process, including the search strategy and screening outcomes, is depicted in a PRISMA 2020 flow diagram (Figure 2).

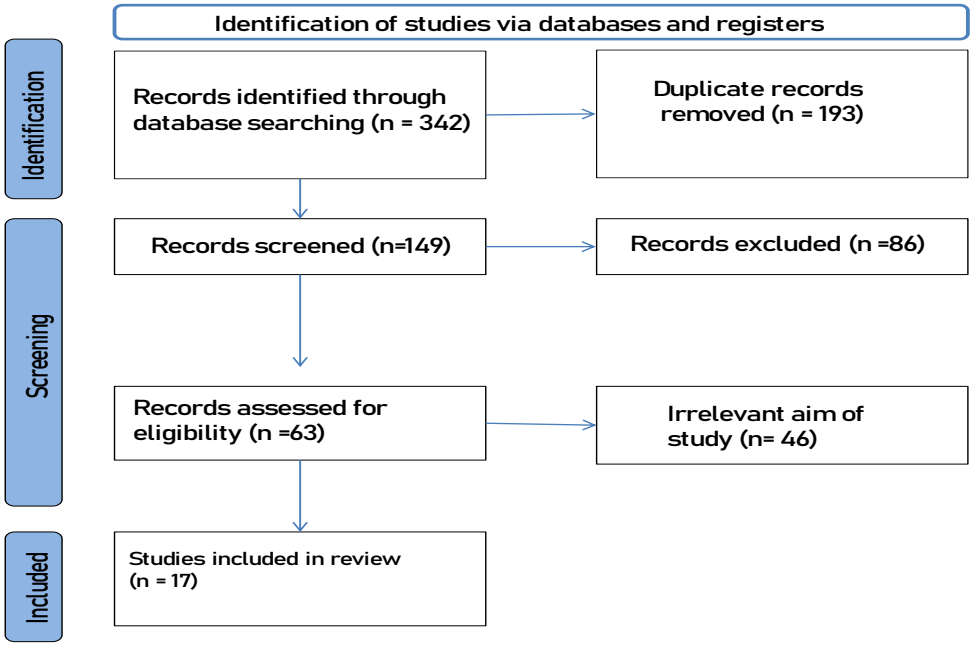


Figure 2: Shows the PRISMA flow diagram illustrating the study selection process

Data extraction

From the included publications, the following data were systematically extracted and tabulated: lead author's name, year of publication, study model or participants, experimental or clinical measurements, daily dose, and observed effects. Any information unrelated to the objectives of the study was excluded from the analysis.

Results

The initial search retrieved 342 publications. After screening titles and abstracts, 193 records were removed due to duplication, and 86 articles were excluded because they were irrelevant or focused on other topics. Ultimately, 17 articles were selected for final evaluation, and their results were compiled in Tables 1 and 2.

Following the initial screening, the extracted information was independently assessed, and any remaining duplicates were excluded. The 17 included studies investigated various medicinal plants from the Zagros region, including *Pistacia atlantica* (n = 4), *Matricaria chamomilla* L. (n = 5), *Capparis spinosa* (n = 4), and *Ferulago angulata* (n = 4). The studies employed both in vivo and in vitro approaches, involving human participants and animal models. Key outcomes measured included histological assessments, semen analysis, sperm parameters, gene expression, hormonal changes, and antioxidant activities.

Overall, these studies explored the effects of Zagros-native medicinal plants on male and female reproductive function, examining parameters such as sperm quality, biochemical markers, hormone levels, apoptosis, gene expression, and antioxidant activity, providing comprehensive insights into their potential therapeutic roles in infertility management.

Table1. Effects of *P. atlantica* and *M. chamomilla* on reproductive systems.(* in vitro study)

Plant	Effects	Part used	Animal / participant	Daily dose	Study measures	Author and year
P. atlantica	Increased (Sperm motility, Sperm count, Sperm viability, protection of germinal, Antioxidant activity epithelium) Decreased (Edema in testis, DNA damage)	Fruit	male rats (busulfan azoospermia)	10 mg/kg	Sperm Parameters Testis Histopathology Antioxidant level	[52]
P. atlantica	Increased (levels of estradiol and progesterone, ratio of the ovary/body weight, High density lipoprotein(HDL)levels in serum, parameters of healthy Graffian follicle, expression of oxytocin level and receptor, number of endometrial glands, thickness of uterine epithelium) Decreased (levels of Low density lipoprotein(LDL) and	Fruit	female rats	20 % (w/w) In food	Hormone levels Reproductive organs weight lipid profile assessment oxidant level	[53]

	Triglyceride (TG), concentration of ovary MDA)					
P. atlantica	Increased (Testosterone Level, Sperm Counts, HDL Levels in Serum, Testicular Capsule Thickness, Expression Of OXT And OXTR Genes) Decreased (Concentration Of Ovary MDA, AST Level in Serum)	Fruit	male rat	20 % (w/w) In food	Weight of the Body and Organs Hormone Levels Sperm Parameters Histomorphometrically Analysis	[54]
P. atlantica	Increased (Blood glucose concentrations (FBS), SOD and CAT activities, number of secondary follicles) Decreased (Numbers of corpus luteum)	Fruit	female rats (STZ diabetic)	200 mg/kg	biochemical In serum parameters Follicular parameters Antioxidant activity	[55]
M. chamomilla	Increased (Ovarian Tissue Quality, Endometrial Tissue Arrangement, Number of	Flower	Virgin adult female rats poly cystic ovarian syndrome(PCOS)model	75 mg/kg	Gonadotropins and Gonadal Steroids Ovarian Morphology	[56]

	Dominant Follicles) Decreased (Ovarian Cysts, Estradiol Levels in Serum, LH Level, FSH Level)					
M. chamomilla	Increased (Progesterone and Dehydroepiandrosterone) Decreased (Survived follicle, ROS level, Estrogen (DHEA), Follicular activity)	Flower	Female mice (ovarian follicles) *	50 µg/ml	follicular morphology and diameter Hormone Levels	[58]
M. chamomilla	Increased (Sperm count, Testosterone level, Sperm motility, Sperm viability, Miller's and Johnson's scores) Decreased (Seminiferous tubules with Apoptotic germ cells)	Flower	male rat (formaldehyde treated)	۵۰۰ mg/kg	Gonadosomatic index Hormonal analysis sperm parameters Histological assessment	[59]
M. chamomilla	Increased (Estrogen, Progesterone concentration) Decreased (Body weight	Flower	female rats	۴۰ mg/kg	Hormones of serum Histological assessment	[60]

	Graafian follicle, Primary follicles)					
M. chamomilla	Decreased (Oligomenorrhea, Hirsutism FBS, Testosterone level)	Flower	Women patiens(PCOS)		biochemical in serum parameters Hormone of serum Clinical signs	[61]

Table2. Effects of Capparis spinosa L and Ferulago angulata on reproductive systems.(*in vitro study)

Plant	Effects	Part used	Animal / participant	Daily dose	Study measures	Author and year
C. spinosa L	Increased (Antioxidant, progressive, motility, Sperm Viability) Decreased (DNA damage)	Leaf and friut	men (semen)*	45ppm	Antioxidant effect Sperm parameters	[62]
C. spinosa L	Increased (Number of corpus lutea, Antral follicle) Decreased (LDL and TG level, FBS, LH, and FSH concentration, Testosterone level)	Aerial parts	Female mice (PCOS Letrozole induction)	50 mg/100g	Hormone of serum Histological assessment	[63]
C. spinosa L	Decreased Testosterone level No change in FSH And LH	Flower bud	Male Rat	100 mg/kg	Hormones of serum	[64]

C. spinosa L	Increased (Testosterone level, testis weight, Sperm motility, hormonal, balance)	Fruit	male rat (STZ diabetic)	30mg/kg	Sperm parameters Testis weight Hormone of serum	[65]
F. angulata	Increased (sperm morphology, Sperm motility, Sperm Viability, Seminiferous tubules, diameter, Johnson's score)	leaves and stems	male rat (STZ diabetic)	400/kg	Sperm parameters Hormones of serum	[66]
F. angulata	Increased (sperm viability, testis weight, Johnson's score, Testosterone level, SOD and GPx activity) Decreased (abnormal sperm, MDA Concentration)	Aerial parts	male rat (Torsion/ Detorsion-Induced)	200 mg/kg	Sperm parameters Hormone of serum Histological assessment Antioxidant activity	[68]
F. Angulata	Increased (sperm motility peroxidation Mate and fertility) Decreased (ROS Concentration, Lipid)	leaves and stems	Male mice (sperm toxicity lead and diazinon	400 mg/kg	Sperm parameters Histological assessment Assessment of ROS Mating and fertility indices	[69]
F. angulata	Increased (Testosterone level, testis weight, Sperm motility,	stem	Male Rats	400 mg/kg	Sperm parameters body weight testis weight	[70]

	sperm viability)				Hormone of serum	

Discussion

Different studies have demonstrated that varying treatment durations and doses of the investigated plants can effectively enhance or regulate fertility.

The dried extract of different subspecies of *Pistacia atlantica* fruit was reported to increase sperm count and motility. Additionally, administration of this extract prevented excessive thinning of the germinal epithelium and enhanced the activity of antioxidant enzymes such as superoxide dismutase (SOD) and catalase. Its antioxidant properties were also linked to protective effects on sperm chromatin quality [52]. In female rats, *P. atlantica* extract increased serum HDL, decreased LDL and triglycerides, reduced malondialdehyde (MDA) levels, and improved follicular parameters, indicating positive effects on reproductive health [53]. Experimental studies on male rats showed that *P. atlantica* enhanced testosterone levels, increased testicular capsule thickness, and exhibited antioxidant effects, thereby supporting spermatogenesis. Furthermore, upregulation of oxytocin gene expression was associated with increased male gamete production [54]. In female rats, administration of *P. atlantica* extract reduced atretic follicles, increased primary and secondary follicles, and improved ovarian tissue health and function [55].

In polycystic ovarian syndrome (PCOS) models, *Matricaria chamomilla* extract promoted the disappearance of ovarian cysts, increased the number of mature follicles, and restored endometrial health. Treatment was accompanied by reductions in estradiol, LH, FSH, and gonadotropin levels [56]. Hydroalcoholic chamomile extract also improved testicular tissue and seminiferous tubule structure, increased germinal epithelium thickness, enhanced SOD activity, and facilitated spermiogenesis in male rats [57]. However, some studies reported inhibitory effects of chamomile flowers on ovarian follicles, including reduced follicle diameter and survival, and decreased estrogen levels, which may impair follicular growth and gametogenesis [58]. Conversely, other studies demonstrated that chamomile extract increased testosterone levels in male rats, improved sperm motility and count, and reduced apoptosis in seminiferous tubules [59]. Investigations into the gonadal-pituitary axis revealed that chamomile extract could alter estrogen and progesterone levels, leading to changes in ovarian follicle numbers and function, and potentially supporting PCOS management [60–61].

Studies on *Capparis spinosa* L. demonstrated that ethanolic extracts of leaves and fruits increased human sperm motility and exhibited antioxidant activity, with leaves showing significantly higher antioxidant potential than fruits [62]. In PCOS mice, *C. spinosa* extract reduced blood glucose and lipid levels, mimicking metformin effects, and improved hormonal balance by decreasing LH, FSH, and testosterone levels while increasing mature follicles, corpora lutea, and eliminating ovarian cysts [63–65]. The plant's phytoestrogen content supports regulation of the pituitary-gonadal axis, favoring proper spermatogenesis and gametogenesis.

Ferulago angulata extract increased serum testosterone, testis weight, improved seminiferous tubule morphology, and enhanced sperm production [66–68]. High doses further increased testis weight, testosterone concentration, and progressive sperm motility, highlighting its potential to support effective spermatogenesis [69–70]. Antioxidant properties of *F. angulata* were also associated with reduced reactive oxygen species (ROS) levels, fewer abnormal sperm, and higher sperm survival rates.

Collectively, these findings indicate that the studied Zagros-native plants exert multifaceted effects on male and female reproductive parameters, primarily through hormonal modulation, antioxidant activity, and enhancement of gamete quality and ovarian/testicular structure.

Study limitations

The primary limitation of this study is the paucity of clinical research, which restricts the direct translation of findings into human applications. Most evidence originates from small-scale, preclinical studies with diverse experimental models, limiting generalizability. Additionally, variations in sample size, dosing regimens, and extraction methods contribute to inconsistencies across studies. These factors underscore the need for well-designed, large-scale clinical trials to generate robust, reliable, and clinically applicable evidence.

Conclusion

The evidence reviewed underscores the potential of medicinal plant extracts in enhancing fertility and reproductive health. By supporting the production of healthy gametes and facilitating conception, these natural compounds may serve as effective complementary interventions alongside conventional infertility

treatments, potentially minimizing associated side effects. Nonetheless, the observed variability in outcomes across studies highlights the need for rigorous, controlled research to validate efficacy and safety. With further investigation, these plants could be safely incorporated as dietary supplements or therapeutic agents, ultimately improving reproductive outcomes and contributing to overall quality of life.

Author Contributions:

Conceptualization: Firoozeh Niazvand; Data curation: Firoozeh Niazvand; Formal analysis: Amirabbas Gharibi, Firoozeh Niazvand; Funding acquisition: Firoozeh Niazvand; Investigation: Amirabbas Gharibi, Firoozeh Niazvand, Mahtab Teimouri; Methodology: Firoozeh Niazvand. Ali Aidy; Project administration: Firoozeh Niazvand; Resources: Amirabbas Gharibi, Firoozeh Niazvand; Software: Amirabbas Gharibi, Ali Aydi; Supervision Firoozeh Niazvand, Mahtab Teimouri; Validation: Firoozeh Niazvand, Mahtab Teimouri, Ali Aydi; Visualization: Mahtab Teimouri,Amirabbas Gharibi; Writing–original draft: Amirabbas Gharibi; Writing–review & editing Amirabbas Gharibi, Mahtab Teimouri

Conflict of interests

The authors declare there are no conflicts of interest.

Ethical considerations

Authors have carefully monitored ethical issues such as text plagiarism, duplicated publication, misconduct, data fabrication, and falsification.

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