Acta Scientific Women's Health (ISSN: 2582-3205)

Volume 8 Issue 6 June 2026

Review Article

Role of Myo-Inositol and N-Acetyl-L-Cysteine in Improving Female Fertility: A Comprehensive Review

Nazis Chavda[1]*, Debabrata Sarkar[2] and Ronak Chhaya[2]

[1]QA/RA Department, BioAni India Pvt. Ltd., India

[2]Research and Development Division, BioAni India Pvt. Ltd., India

***Corresponding Author:** Nazis Chavda, QA/RA Department, BioAni India Pvt. Ltd., Lilapur, Ahmedabad, Gujarat, India.

Received: July 29, 2026

Published: August 07, 2026

DOI: 10.31080/ASWH.2026.08.0758

Abstract

Female infertility is a complex reproductive disorder affected by endocrine, metabolic, and oxidative stress-related abnormalities, with polycystic ovary syndrome (PCOS) representing one of the leading causes of anovulatory infertility. Amplifying evidence from randomized clinical trials, systematic reviews, and meta-analyses indicates that insulin resistance, oxidative stress, and chronic inflammation play central roles in compromised follicular development, lowered oocyte capacity, and reduced reproductive results. As a result, therapeutic approaches that focus on these basic mechanisms have obtained significant interest as additional approaches to typical fertility treatments. Myo-inositol has evolved as an effective insulin-sensitizing agent that controls intracellular signalling involved in glucose metabolism, ovarian steroidogenesis, follicular maturation, and ovulation. Clinical studies consistently reveal improvements in menstrual regularity, ovulatory function, oocyte quality, and assisted reproductive technology results, primarily among women with PCOS. N-acetyl-L-cysteine, a precursor of glutathione, uses strong antioxidant and anti-inflammatory impacts by lowering oxidative stress, elevating cellular redox homeostasis, and improving insulin sensitivity. Developing clinical evidence further suggests that N-acetyl-L-cysteine may enhance ovulation, endocrine profiles, and pregnancy results while supporting metabolic approaches in women with infertility. This extensive review precisely examines the current evidence regarding the physiological roles, molecular mechanisms, clinical efficacy, and therapeutic potential of myo-inositol and N-acetyl-L-cysteine in enhancing female fertility. It also discusses the additional actions of these compounds, discusses available clinical evidence, recognizes current limitations, and highlights future research directions to support evidence-based and specific fertility management.

Keywords: Myo-inositol; N-acetyl-L-cysteine; Female infertility; Polycystic ovary syndrome; Insulin resistance; Oxidative stress

Abbreviations

ART: Assisted Reproductive Technology; Akt: Protein Kinase B; ATP: Adenosine Triphosphate; DAG: Diacylglycerol; DNA: Deoxyribonucleic Acid; FSH: Follicle-Stimulating Hormone; GLUT4: Glucose Transporter Type 4; GSH: Glutathione; IL: Interleukin; IL-6: Interleukin-6; IP3: Inositol 1,4,5-Trisphosphate; IRS: Insulin Receptor Substrate; LH: Luteinizing Hormone; MI: Myo-Inositol; NAC: N-Acetyl-L-Cysteine; NF-κB: Nuclear Factor-kappa B; PCOS: Polycystic Ovary Syndrome; PI3K: Phosphoinositide 3-Kinase; PKC: Protein Kinase C; ROS: Reactive Oxygen Species; SHBG: Sex Hormone-Binding Globulin; TNF-α: Tumor Necrosis Factor-alpha.

Introduction

Female infertility is a major reproductive health concern impacting millions of women worldwide and contributes significantly to the global burden of infertility [5,17,21]. It is a complex condition affected by endocrine, metabolic, genetic, environmental, and lifestyle practices [5,17,21]. From these, polycystic ovary syndrome (PCOS) is the most common endocrine disorder related with anovulatory infertility and is frequently associated by insulin resistance, hyperandrogenism, chronic low-grade inflammation, and oxidative stress [4,5,17,21]. These interconnected abnormalities impair follicular development, compromise oocyte quality, disrupt ovulation, and ultimately reduce the probability of successful conception [4,6,17,18]. Conventional management of female infertility includes lifestyle modification, ovulation induction, insulin-sensitizing agents, and assisted reproductive technologies (ART) [11,17,21]. Although these approaches have improved reproductive results, they do not always address the underlying metabolic and oxidative disturbances that contribute to ovarian dysfunction [4,6,17]. Consequently, increasing attention has been directed toward adjunctive therapies capable of targeting these pathogenic mechanisms while improving overall reproductive function [3,5,6,17]. Among the nutritional and metabolic interventions investigated, myo-inositol (MI) and N-acetyl-L-cysteine (NAC) have emerged as promising therapeutic agents because of their complementary biological activities [3,5,8,17]. Myo-inositol plays an important role in insulin signalling, glucose metabolism, follicle-stimulating hormone (FSH) signalling, and ovarian steroidogenesis, thereby supporting follicular maturation, ovulation, and oocyte competence [5,12,17,18,25]. In contrast, N-acetyl-L-cysteine functions primarily as a precursor of glutathione, enhancing antioxidant defense, reducing oxidative stress, enhancing mitochondrial function, and contributing to better metabolic homeostasis [4,6,8,10]. Clinical studies and systematic reviews have demonstrated that these interventions may improve menstrual cyclicity, ovulation, endocrine parameters, oocyte quality, and pregnancy outcomes, particularly in women with PCOS [3-5,10,11,17].

Pathophysiological Basis of Female Infertility

Female fertility is regulated by a complex interaction of endocrine, metabolic, and cellular processes that ensure normal follicular development, ovulation, fertilization, and embryo implantation [5,17,18]. Disruption of these physiological processes may impair reproductive function and contribute to infertility [5,17,21]. Among the various etiological factors, endocrine imbalance, insulin resistance, oxidative stress, chronic inflammation, and mitochondrial dysfunction are considered the major mechanisms underlying female infertility, particularly in women with polycystic ovary syndrome (PCOS) [4-6,17,21].

Endocrine and metabolic dysregulation

Normal ovarian function depends on the coordinated action of the hypothalamic-pituitary-ovarian axis [17,18,21]. Disturbances in this hormonal network can impair follicular growth and ovulation [17,18,21]. In women with PCOS, insulin resistance is frequently accompanied by compensatory hyperinsulinemia, which stimulates ovarian androgen production and suppresses hepatic synthesis of sex hormone-binding globulin [15,17,21,22]. The resulting hyperandrogenic environment disrupts follicular maturation, leading to anovulation and reduced fertility [15,17,21,23]. Furthermore, altered insulin signalling adversely affects glucose metabolism within ovarian tissues, compromising oocyte development and reproductive competence [5,15,17,18,22].

Oxidative stress and chronic inflammation

Oxidative stress arises when the generation of reactive oxygen species exceeds the capacity of endogenous antioxidant defense systems [4,6,8]. Excessive oxidative stress damages lipids, proteins, and nucleic acids within ovarian cells, impairing granulosa cell function and reducing oocyte quality [4,6,8,18]. In parallel, chronic low-grade inflammation contributes to ovarian dysfunction through the release of inflammatory mediators that further exacerbate oxidative damage [4,6,8,10]. The combined effects of oxidative stress and inflammation create an unfavourable follicular microenvironment, reducing ovulatory potential and reproductive success [4,6,8,10].

Mitochondrial dysfunction

Mitochondria are the primary source of cellular energy required for oocyte maturation, fertilization, and early embryonic development [6,18,24]. Impaired mitochondrial function reduces adenosine triphosphate (ATP) production and increases intracellular oxidative stress, leading to defective meiotic progression and diminished oocyte competence [6,8,18].

Mitochondrial dysfunction has therefore been recognized as an important contributor to poor embryo quality and reduced fertility outcomes [6,18,24].

Therapeutic implications

The pathogenesis of female infertility involves multiple interconnected mechanisms rather than a single pathological process [4,5,6,17]. Consequently, therapeutic approaches targeting both metabolic abnormalities and oxidative stress may provide greater clinical benefits than treatments focused on hormonal regulation alone [3-6,17]. Myo-inositol improves insulin signalling and ovarian function, whereas N-acetyl-L-cysteine enhances antioxidant defences by replenishing intracellular glutathione and reducing oxidative stress [3-5,8,17]. Their complementary mechanisms provide a strong biological rationale for their use as adjunctive therapies in women with infertility, particularly those with PCOS [3,5,8,10,17].

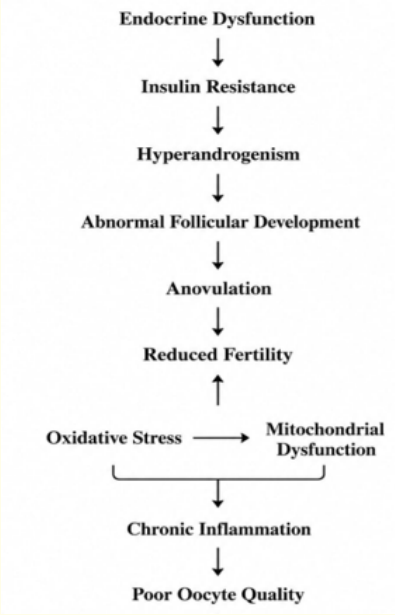

Figure 1: Pathophysiological Mechanisms Underlying Female Infertility.

Role of myo-inositol in female fertility

Myo-inositol (MI) is a naturally occurring carbocyclic polyol that plays an essential role in cellular signaling and reproductive physiology [5,17,18,25]. As a precursor of phosphatidylinositol and inositol phosphates, MI participates in multiple intracellular signaling pathways involved in glucose metabolism, insulin action, calcium homeostasis, and ovarian function [5,17,18,25]. Owing to its insulin-sensitizing properties and regulatory role in follicular development, MI has emerged as a promising therapeutic option for improving female fertility, particularly in women with polycystic ovary syndrome (PCOS) [5,11,17,21,25].

Biological role of myo-inositol

Myo-inositol is an important component of the phosphoinositide signaling pathway and functions as a second messenger in follicle-stimulating hormone (FSH) signaling [5,17,18,25]. It regulates ovarian steroidogenesis, follicular maturation, and oocyte development [5,12,17,18]. Adequate intracellular concentrations of MI are essential for maintaining normal ovarian physiology and supporting successful ovulation [12,17,18,23]. Disturbances in MI metabolism have been associated with impaired insulin signaling and reduced reproductive function [5,15,17,21].

Mechanisms of action

The therapeutic effects of MI are primarily attributed to its ability to improve insulin sensitivity and restore metabolic homeostasis [5,15,17,21,22]. Enhanced insulin signalling reduces circulating insulin levels, thereby decreasing ovarian androgen production and improving hormonal balance [15,17,21,22]. These changes promote normal follicular growth, facilitate ovulation, and improve menstrual regularity [9,15,17,21,23]. In addition to its metabolic actions, MI contributes to calcium-mediated intracellular signalling that is required for oocyte maturation and fertilization [12,18,25]. Improved calcium regulation supports meiotic progression and enhances oocyte competence [12,18,24,25]. By improving both metabolic and cellular functions, MI creates a more favourable ovarian environment for successful reproduction [5,17,18,21].

Myo-inositol exerts its reproductive effects primarily through its role as a precursor of phosphatidylinositol phosphates, which function as second messengers in multiple intracellular signalling pathways. Following insulin receptor activation, phosphatidylinositol-3-kinase (PI3K) catalyses the phosphorylation of phosphatidylinositol lipids, leading to activation of protein kinase B (Akt). Activation of the PI3K/Akt pathway enhances translocation of glucose transporter-4 (GLUT4) to the cell membrane, thereby increasing glucose uptake in insulin-sensitive tissues, including ovarian granulosa cells. Restoration of insulin sensitivity reduces compensatory hyperinsulinaemia,

resulting in decreased ovarian androgen synthesis and improved follicular development [5,15,17,22].

In ovarian follicles, myo-inositol also functions as an essential intracellular mediator of follicle-stimulating hormone (FSH) receptor signalling. Binding of FSH to its receptor activates phospholipase C-mediated hydrolysis of phosphatidylinositol bisphosphate, generating inositol trisphosphate (IP3) and diacylglycerol (DAG). IP3 stimulates calcium release from the endoplasmic reticulum, whereas DAG activates protein kinase C (PKC). The coordinated activation of these signalling molecules regulates granulosa cell proliferation, steroidogenesis, aromatase activity, and estrogen biosynthesis, thereby promoting follicular maturation and ovulation [5,12,17,18,23].

Calcium-dependent signalling mediated by myo-inositol is equally important during oocyte maturation. Oscillatory intracellular calcium release regulates meiotic spindle formation, chromosome alignment, cortical granule exocytosis, fertilization, and early embryonic cleavage. Adequate intracellular myo-inositol concentrations therefore improve oocyte developmental competence and increase embryo implantation potential, particularly in women undergoing assisted reproductive technologies [12,18,24,25].

Furthermore, restoration of metabolic homeostasis by myo-inositol decreases circulating luteinizing hormone (LH) mediated androgen production while increasing sex hormone-binding globulin (SHBG) synthesis, thereby reducing free testosterone concentrations. The combined improvement in endocrine balance, insulin sensitivity, and intracellular signalling contributes to restoration of ovulation and enhancement of spontaneous pregnancy rates in women with polycystic ovary syndrome [9,15,22,23].

Myo-Inositol in women with PCOS

PCOS is characterized by insulin resistance and hyperandrogenism, both of which adversely affect ovarian function [15,17,21,22]. By improving insulin sensitivity, MI indirectly reduces androgen production and promotes normal follicular maturation [15,17,21,22]. As a result, many women receiving MI experience improved ovulation and better reproductive outcomes [2,9,11,16,23]. In addition, improved metabolic control may enhance the effectiveness of conventional fertility treatments and reduce the need for intensive ovarian stimulation in selected patients [2,11,24,25].

Molecular mechanisms underlying improvement of female fertility

Myo-inositol contributes to female fertility through coordinated regulation of metabolic, endocrine, and cellular pathways. Improved insulin signalling decreases ovarian androgen production, while enhanced FSH receptor signalling promotes granulosa cell differentiation and follicular growth. Simultaneously, intracellular calcium mobilization supports meiotic progression and fertilization, whereas improved glucose metabolism maintains mitochondrial ATP production required for oocyte maturation. Collectively, these molecular events improve follicular quality, ovulatory function, embryo competence, and implantation potential [5,17,18,21,25].

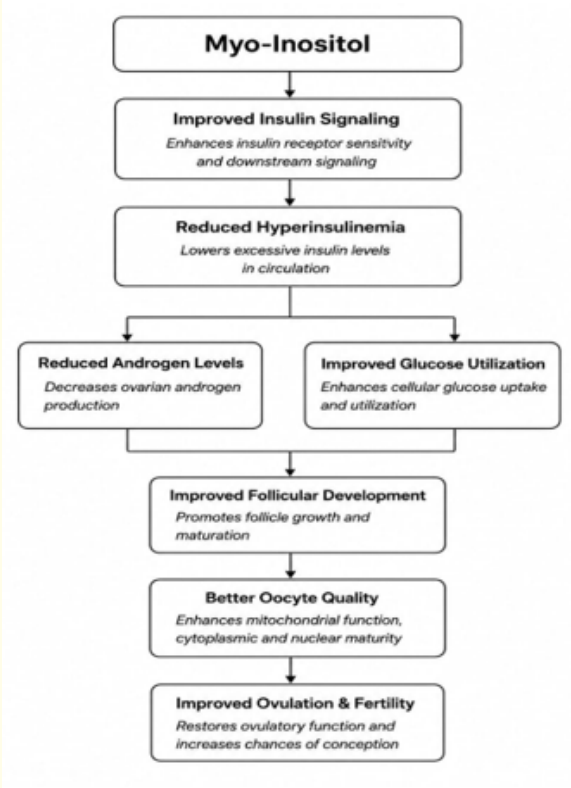

Figure 2: Mechanisms of Myo-Inositol in Female Fertility.

Role of N-Acetyl-L-Cysteine in female fertility

N-acetyl-L-cysteine (NAC) is a thiol-containing compound and a precursor of glutathione (GSH), one of the body's most important intracellular antioxidants [4,6,8,10]. By replenishing glutathione stores, NAC helps maintain cellular redox balance, protects ovarian tissues from oxidative damage, and supports normal reproductive function [4,6,8]. Beyond its antioxidant properties, NAC also exhibits anti-inflammatory and insulin-sensitizing effects, making it a promising adjunctive therapy for women with infertility, particularly those with polycystic ovary syndrome (PCOS) [3,4,8,10].

Antioxidant mechanisms of NAC

Oxidative stress plays a significant role in female infertility by impairing follicular development, damaging oocytes, and disrupting the ovarian microenvironment [4,6,8,10]. NAC reduces oxidative stress by increasing intracellular glutathione levels and scavenging reactive oxygen species (ROS) [4,6,8]. This enhanced antioxidant defense protects granulosa cells and oocytes from oxidative injury, thereby supporting follicular growth and improving reproductive potential [4,6,8,10].

N-acetyl-L-cysteine (NAC) serves as a bioavailable precursor of the amino acid L-cysteine, the rate-limiting substrate required for intracellular glutathione (GSH) synthesis. After cellular uptake, NAC is rapidly deacetylated to cysteine, which subsequently participates in glutathione biosynthesis through the sequential enzymatic actions of γ-glutamylcysteine synthetase and glutathione synthetase. Increased intracellular glutathione replenishes the endogenous antioxidant defense system and enhances detoxification of reactive oxygen species (ROS), including superoxide anions, hydrogen peroxide, and hydroxyl radicals [3,4,6,8].

Within the ovary, excessive ROS generation disrupts granulosa cell function, induces mitochondrial dysfunction, promotes lipid peroxidation, and causes oxidative DNA damage in developing oocytes. NAC limits these deleterious effects by restoring intracellular redox homeostasis, preserving mitochondrial membrane integrity, and preventing oxidative stress-induced apoptosis of granulosa cells. Consequently, follicular development is maintained under physiological conditions, resulting in improved oocyte maturation and enhanced reproductive competence [4,6,8,10].

Beyond its direct antioxidant activity, NAC regulates several intracellular signalling pathways involved in inflammation and cellular survival. Increased glutathione availability suppresses activation of nuclear factor-kappa B (NF-κB), a transcription factor responsible for the expression of numerous pro-inflammatory cytokines, including tumour necrosis factor-alpha (TNF-α), interleukin-6 (IL-6), and interleukin-1β (IL-1β). Downregulation of these inflammatory mediators reduces chronic ovarian inflammation, preserves granulosa cell viability, and supports normal follicular growth [4,6,8].

NAC also improves mitochondrial bioenergetics by reducing oxidative injury to mitochondrial DNA and maintaining ATP synthesis required for oocyte maturation and early embryonic development. Improved mitochondrial function decreases apoptosis and enhances cytoplasmic maturation of oocytes, ultimately improving embryo developmental potential and implantation success [6,8,10].

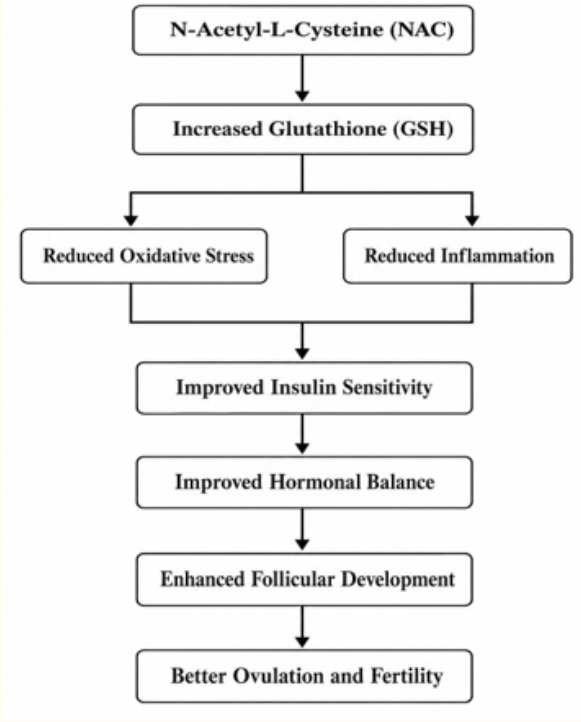

Figure 3: Mechanism of N-acetyl-L-Cysteine in Female fertility.

Effects on metabolic and endocrine function

In addition to its antioxidant properties, NAC positively influences glucose metabolism and endocrine function by improving insulin sensitivity [3,4,8,10]. Oxidative stress is known to impair insulin receptor signalling through activation of stress-associated kinases that inhibit insulin receptor substrate (IRS) phosphorylation [4,6,8]. By reducing intracellular oxidative stress, NAC restores insulin receptor responsiveness and improves glucose utilization in peripheral tissues [3,4,8,10]. Reduced circulating insulin concentrations subsequently decrease ovarian androgen synthesis, improve sex hormone-binding globulin (SHBG) production, and normalize endocrine function in women with polycystic ovary syndrome [1,3,4,8].

Lower androgen concentrations facilitate normal follicular recruitment and granulosa cell differentiation, thereby improving ovulatory function and menstrual cyclicity. Simultaneously, reduced oxidative stress preserves steroidogenic enzyme activity within ovarian follicles, resulting in improved estrogen production and follicular maturation. Clinical investigations have demonstrated improvements in ovulation rates, endocrine parameters, and spontaneous pregnancy following NAC supplementation, particularly in women with insulin-resistant PCOS [1,3,4,10].

Emerging evidence further suggests that NAC may improve endometrial receptivity by reducing oxidative injury and inflammatory signalling within endometrial tissue. Preservation of a favourable uterine microenvironment may facilitate embryo implantation and contribute to improved clinical pregnancy outcomes. Although additional studies are required to confirm these mechanisms, current evidence supports the use of NAC as an adjunctive therapy for improving female reproductive function [4,6,8].

Molecular mechanisms underlying improvement of female fertility

The beneficial effects of NAC on female fertility arise from the coordinated regulation of oxidative stress, inflammation, mitochondrial function, and metabolic homeostasis. By replenishing intracellular glutathione, suppressing ROS generation, inhibiting NF-κB-mediated inflammatory responses, improving insulin signalling, and preserving mitochondrial ATP production, NAC creates a favourable ovarian microenvironment that supports granulosa cell survival, follicular maturation, oocyte competence, fertilization, and embryo implantation. These complementary molecular mechanisms provide the biological rationale for the therapeutic application of NAC in women with infertility, particularly those with polycystic ovary syndrome and oxidative stress-associated reproductive dysfunction [3,4,6,8,10].

Combined Role of Myo-Inositol and N-Acetyl-L-Cysteine in female fertility

Myo-inositol (MI) and N-acetyl-L-cysteine (NAC) possess distinct yet complementary mechanisms of action that collectively address the major pathophysiological factors contributing to female infertility [3,5,8,17,21]. While MI primarily improves insulin signalling, ovarian steroidogenesis, and follicular maturation, NAC enhances intracellular antioxidant capacity, reduces oxidative stress, and modulates inflammatory responses [3,4,5,8,17]. Their combined administration therefore targets both metabolic dysfunction and oxidative damage, providing a comprehensive therapeutic approach for improving reproductive health, particularly in women with polycystic ovary syndrome (PCOS) [3,4,5,10,17].

Complementary mechanisms of action

The therapeutic rationale for combining MI and NAC is based on their ability to influence different but interconnected biological pathways [3,5,8,17]. MI restores insulin sensitivity and promotes normal follicular development by improving intracellular glucose utilization and follicle-stimulating hormone (FSH) signalling [5,15,17,18,22]. In contrast, NAC replenishes intracellular glutathione, protects ovarian cells against oxidative injury, and improves mitochondrial function [4,6,8,10]. Together, these actions help restore hormonal balance, improve the ovarian microenvironment, and support normal ovulation [3,5,8,10,17]. The combination also addresses chronic low-grade inflammation, which frequently accompanies insulin resistance and oxidative stress in women with PCOS [4,6,8,17]. By simultaneously improving metabolic homeostasis and reducing oxidative damage, MI and NAC may enhance overall ovarian function more effectively than either intervention alone [3,5,8,10,17].

Benefits of combination therapy

Clinical evidence indicates that combination therapy with MI and NAC may provide greater improvements in reproductive outcomes than monotherapy in selected patient populations [3,10]. Reported benefits include improved menstrual regularity, increased ovulation rates, enhanced insulin sensitivity, reduced androgen concentrations, and better endocrine profiles [3,10,15,17].

Improvements in follicular development, oocyte quality, and pregnancy outcomes have also been described, particularly among women undergoing fertility treatment [2,3,10,24]. In assisted reproductive technology (ART), optimization of both metabolic and oxidative status before ovarian stimulation may improve ovarian response and support embryo development [12,18,24]. Although available studies are encouraging, differences in treatment protocols and patient characteristics should be considered when interpreting clinical outcomes [4,10,11].

Molecular basis of synergistic action of Myo-Inositol and N-Acetyl-L-Cysteine

The therapeutic efficacy of combining myo-inositol (MI) and N-acetyl-L-cysteine (NAC) arises from their ability to simultaneously target the major pathophysiological mechanisms responsible for female infertility. While MI primarily restores insulin-mediated intracellular signalling and ovarian endocrine function, NAC predominantly protects ovarian tissues from oxidative stress and chronic inflammation. Together, these compounds improve the metabolic, hormonal, and cellular environment required for normal folliculogenesis and successful reproduction [3,5,8,17,21].

At the molecular level, MI activates phosphatidylinositol-dependent insulin signalling pathways that enhance glucose uptake through GLUT4 translocation, thereby reducing hyperinsulinaemia and ovarian androgen synthesis. Simultaneously, NAC replenishes intracellular glutathione concentrations, scavenges reactive oxygen species, and suppresses activation of nuclear factor-kappa B (NF-κB), leading to reduced production of inflammatory cytokines including TNF-α and IL-6. These complementary mechanisms restore ovarian homeostasis by improving insulin sensitivity, reducing oxidative injury, and preserving granulosa cell function [4,5,8,15,17]. The combined improvement in metabolic regulation and antioxidant defense promotes normal follicular recruitment, enhances granulosa cell proliferation, improves steroidogenesis, and supports oocyte maturation through maintenance of mitochondrial ATP production and intracellular calcium signalling. Consequently, women receiving combination therapy may demonstrate improved ovulation rates, superior oocyte quality, enhanced embryo development, and increased implantation potential compared with monotherapy [5,6,10,18,24]. Furthermore, restoration of endocrine balance through decreased circulating insulin and androgen concentrations creates a more favourable follicular microenvironment, while simultaneous reduction of oxidative stress minimizes DNA damage and apoptosis within developing oocytes. This integrated therapeutic approach addresses both the metabolic and oxidative abnormalities characteristic of polycystic ovary syndrome (PCOS), thereby providing a strong biological rationale for combined supplementation with MI and NAC in women experiencing infertility [1,4,6,17,25].

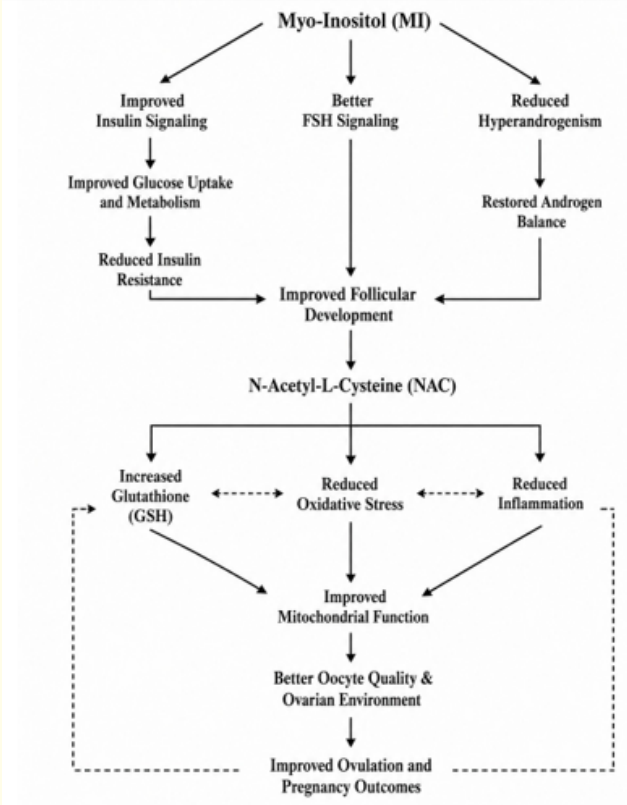

Figure 4: Synergistic Actions of Myo-Inositol and N-Acetyl-L-Cysteine.

Parameter	Myo-Inositol	N-Acetyl-L-Cysteine	Combined Effect
Primary target	Insulin signaling	Oxidative stress	Metabolic + oxidative balance
Main mechanism	PI3K/Akt activation	Glutathione synthesis	Synergistic restoration of ovarian function
Cellular target	Granulosa cells	Granulosa cells and mitochondria	Entire ovarian microenvironment
Hormonal effect	↓ Insulin, ↓ Androgen	↓ Insulin resistance	Improved endocrine profile
Oxidative stress	Mild reduction	Strong antioxidant	Significant reduction
Inflammatory pathway	Indirect	NF-κB inhibition	Reduced inflammatory cytokines
Oocyte quality	Improved maturation	Reduced oxidative damage	Better developmental competence

Table 1

Conclusion

Female infertility is a multifactorial disorder associated with endocrine abnormalities, insulin resistance, oxidative stress, chronic inflammation, and mitochondrial dysfunction, particularly in women with polycystic ovary syndrome (PCOS). These interconnected mechanisms contribute to impaired folliculogenesis, ovulation defects, and reduced reproductive potential, making metabolic and oxidative regulation important therapeutic targets [4,6,17,21]. Myo-inositol (MI) acts as an insulin-sensitizing molecule by improving intracellular insulin signalling, restoring ovarian function, promoting follicular development, and supporting normal ovulation. N-acetyl-L-cysteine (NAC) enhances antioxidant defence through glutathione replenishment, reduces oxidative stress and inflammation, and protects mitochondrial function, thereby improving the ovarian environment [3,5,8,15,18]. The combination of MI and NAC provides complementary therapeutic effects by simultaneously improving insulin sensitivity, reducing oxidative damage, supporting oocyte quality, and enhancing reproductive outcomes. Clinical studies have reported improvements in menstrual regularity, ovulation frequency, pregnancy rates, and assisted reproductive outcomes, especially in women with insulin-resistant PCOS [1,3,5,10,24]. However, further large-scale randomized controlled trials are required to determine optimal dosage, treatment duration, long-term safety, and effectiveness across different infertility conditions. Overall, MI and NAC represent promising complementary agents for improving female fertility by targeting key metabolic and oxidative pathways involved in infertility [6,17,21,25].

Bibliography

1. Ghomian N., *et al*. "Comparison of Pregnancy Rate Between Clomiphene Citrate Alone and Clomiphene Citrate Combined with N-Acetylcysteine in Infertile Women with Polycystic Ovary Syndrome: A Randomized Controlled Trial". *International Journal of Women's Health and Reproduction Sciences* 6.3 (2018): 307-312.

2. Mozafari ME., *et al*. "The Effect of Myo-Inositol and Folic Acid Supplementation on Fertility Outcomes in Infertile Women with Polycystic Ovary Syndrome". *Journal of Ovarian Research* 18.1 (2025): 1-10.

3. Sacchinelli A., *et al*. "The Efficacy of Inositol and N-Acetyl Cysteine Administration (Ovaric HP) in Improving the Ovarian Function in Infertile Women with PCOS with or without Insulin Resistance". *International Journal of Endocrinology* 2014 (2014): 141020.

4. Thakker D., *et al*. "N-Acetylcysteine for Polycystic Ovary Syndrome: A Systematic Review and Meta-Analysis of Randomized Controlled Clinical Trials". *Obstetrics and Gynecology International* 2015 (2015): 817849.

5. Gambioli R., *et al*. "Myo-Inositol as a Key Supporter of Fertility and Physiological Gestation". *Pharmaceuticals* 14.6 (2021): 504.

6. Shang Y., *et al*. "Antioxidants and Fertility in Women with Ovarian Aging: A Systematic Review and Meta-Analysis". *Redox Biology* 78 (2024): 103418.

7. Nemati M., *et al*. "Effect of Myo-Inositol and N-Acetyl-L-Cysteine on Processed Human Spermatozoa for Use in Modern Methods of Fertility Treatment". *Journal of Shahrekord University of Medical Sciences* 22.2 (2020): 53-60.

8. Yifu P. "A Review of Antioxidant N-Acetylcysteine in Addressing Polycystic Ovary Syndrome". *Gynecological Endocrinology* 40.1 (2024): 2381498.

9. Regidor PA and Adolf E Schindler. "Myo-Inositol as a Safe and Alternative Approach in the Treatment of Infertile PCOS Women: A German Observational Study". *International Journal of Endocrinology* 2016 (2016): 9537632.

10. Saxena S., *et al*. "Effects of Myo-Inositol and N-Acetylcysteine in Women with Polycystic Ovary Syndrome". *BMC Endocrine Disorders* 24.1 (2024): 44.

11. Bevilacqua A., *et al*. "Myo-Inositol and D-Chiro-Inositol in Improving Reproductive Outcomes in Women with Polycystic Ovary Syndrome: A Systematic Review". *International Journal of Molecular Sciences* 24.9 (2023): 7932.

12. Unfer V., *et al*. "Myo-Inositol Rather than D-Chiro-Inositol Is Able to Improve Oocyte Quality in Intracytoplasmic Sperm Injection Cycles: A Prospective, Controlled, Randomized Trial". *European Review for Medical and Pharmacological Sciences* 15.4 (2011): 452-457.

13. Nestler JE., *et al*. "Ovulatory and Metabolic Effects of D-Chiro-Inositol in the Polycystic Ovary Syndrome". *The New England Journal of Medicine* 340.17 (1999): 1314-1320.

14. Nordio M and Emiliano Proietti. "The Combined Therapy with Myo-Inositol and D-Chiro-Inositol Reduces the Risk of Metabolic Disease in PCOS Women". *European Review for Medical and Pharmacological Sciences* 16.5 (2012): 575-581.

15. Genazzani AR., *et al*. "Myo-Inositol Administration Positively Affects Hyperinsulinemia and Hormonal Parameters in Overweight Patients with Polycystic Ovary Syndrome". *Gynecological Endocrinology* 24.3 (2008): 139-144.

16. Facchinetti F., *et al*. "Short-Term Effects of Myo-Inositol in Women with Polycystic Ovary Syndrome: A Randomized Clinical Trial". *European Review for Medical and Pharmacological Sciences* 17.3 (2013): 298-304.

17. Laganà AS., *et al*. "Inositol in Polycystic Ovary Syndrome: Restoring Fertility Through a Physiological Approach". *International Journal of Endocrinology* 2018 (2018): 9528050.

18. Chiu TTY., *et al*. "Myo-Inositol in Oocyte Development and Fertility: A Systematic Review". *Reproductive Biology and Endocrinology* 15.1 (2017): 1-12.

19. Artini PG., *et al*. "Role of Myo-Inositol and Antioxidants in Improving Female Reproductive Function". *Gynecological Endocrinology* 33.6 (2017): 464-467.

20. Carlomagno G and Vittorio Unfer. "Inositol Safety: Clinical Evidence and Future Perspectives". *European Review for Medical and Pharmacological Sciences* 15.8 (2011): 931-936.

21. Regidor P A., *et al*. "Management of Women with Polycystic Ovary Syndrome Using Myo-Inositol: Clinical Evidence and Future Perspectives". *International Journal of Endocrinology* 2018 (2018): 8796503.

22. Costantino D., *et al*. "Metabolic and Hormonal Effects of Myo-Inositol in Women with Polycystic Ovary Syndrome: A Double-Blind Trial". *European Review for Medical and Pharmacological Sciences* 13.2 (2009): 105-110.

23. Papaleo E., *et al*. "Myo-Inositol in Patients with Polycystic Ovary Syndrome: A Novel Method for Ovulation Induction". *Gynecological Endocrinology* 23.12 (2007): 700-703.

24. Minozzi M., *et al*. "The Combined Use of Myo-Inositol and Folic Acid in Women with Polycystic Ovary Syndrome Undergoing Assisted Reproduction". *European Review for Medical and Pharmacological Sciences* 15.4 (2011): 509-514.

25. Unfer V and Antonio Simone Laganà. "Myo-Inositol: From Basic Science to Clinical Practice in Polycystic Ovary Syndrome". *International Journal of Endocrinology* 2017 (2017): 6846285.