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Natural Chemical Constituents and Polymer Used in to Reduce PCOS Pain

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ABSTRACT

The complex metabolic and endocrine disorder known as polycystic ovarian syndrome (PCOS) is characterised by anovulation, infertility, obesity, insulin resistance, and polycystic ovaries. Factors that predispose women to polycystic ovarian syndrome encompass dietary and lifestyle decisions, environmental pollutants, genetic predisposition, gut dysbiosis, alterations in neuroendocrine function, and excess adiposity. Hyperinsulinemia, oxidative stress, hyperandrogenism, inadequate folliculogenesis, and irregular menstrual periods are symptoms that may arise from these variables, potentially contributing to an escalation of metabolic syndrome. Pathogenic dysbiosis of the gut microbiota may have a role in the aetiology of polycystic ovarian syndrome (PCOS). Immature oocytes, insulin resistance, hyperandrogenism, inflammation, oxidative stress, and resveratrol are pathological features of PCOS that may be ameliorated by supplementation with natural compounds such as polyphenols, quercetin, resveratrol, flavonoids, vitamin C, gamma-linolenic acid, piperine, and omega-3 fatty acids, along with natural and semi-synthetic polymers. This review encapsulates the current understanding of the efficacy of natural chemical supplementation in the treatment of PCOS.

Keywords- Chemical constituent, Polymer, PCOS, pain relief.

I. INTRODUCTION

Polycystic ovarian syndrome (PCOS) is characterised by elevated testosterone levels, irregular menstruation, and/or small cysts on one or both ovaries, constituting a complex medical condition. The illness may present with both morphological (polycystic ovaries) and biochemical (hyperandrogenemia) signs. A sign of polycystic ovary syndrome (PCOS) is hyperandrogenism, which may result in irregular menstrual periods, anovulation, ovarian microcysts, and inhibition of follicular development[1].

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Polycystic Ovary Syndrome (PCOS) is a multifaceted disorder affecting at least 7% of adult women. Approximately 5 million American women of reproductive age are afflicted with polycystic ovarian syndrome (PCOS), as reported by the NIH Office for Disease Prevention. The identification and management of polycystic ovarian syndrome (PCOS) incurs an annual expense over $4 billion for the American healthcare system[2].

Polycystic ovary syndrome (PCOS) is the most common endocrine condition among women of reproductive age in the United States, impacting around 5–10% of women aged 18 to 44 [3]. A diagnosis of polycystic ovarian syndrome (PCOS) is prevalent among women who pursue medical care for issues including obesity, acne, amenorrhoea, hirsutism, and infertility. Cystic fibrosis, endometrial cancer, dyslipidaemia, and type 2 diabetes mellitus are all more prevalent in women with polycystic ovarian syndrome[4,5].

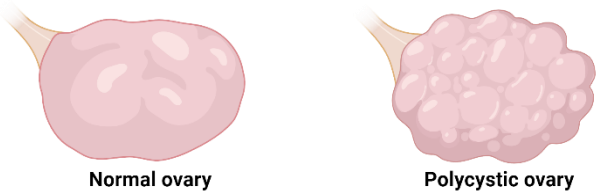

Fig.1: Difference between normal ovary and polycystic ovary

Etiology

Due to its complex and interrelated pathophysiology, identifying the causes of this multifactorial disease is difficult. Environmental toxins, suboptimal dietary and lifestyle choices, genetic factors, excessive adiposity, and intestinal dysbiosis may all contribute to polycystic ovarian syndrome (PCOS) [6]. The emergence of insulin resistance, the cessation of partial folliculogenesis, the increase of metabolic syndrome, and the continual low-grade secretion of inflammatory mediators from leukocytes are all potential consequences of these factors. Numerous studies indicate that environmental pollutants, such as pesticides, heavy metals, and endocrine-disrupting chemicals (EDCs), have significant adverse effects on human health and fertility. There is increasing evidence that environmental pollutants affect PCOS. Embracing a better lifestyle serves as the primary defence against polycystic ovarian syndrome (PCOS), yet it should not replace pharmacological treatments. Clinical guidelines for numerous diseases and ailments recommend the following lifestyle modifications: abstaining from smoking, maintaining a healthy weight, consuming a nutritious diet, and engaging in regular physical activity[7]. These parameters are essential in the prevention and treatment of metabolic disorders. Specific genes, gene interactions, or environmental variables may affect an individual's predisposition to develop polycystic ovarian syndrome (PCOS), a multifaceted and polygenic condition. Numerous genetic studies have associated various symptoms of polycystic ovarian syndrome (PCOS) with a limited set of genes exhibiting mutations or single-nucleotide polymorphisms. All mutations and genes influencing the ovaries are linked to polycystic ovarian syndrome (PCOS) [8]. Inflammation and alterations in gut permeability can affect a host's health, with gut dysbiosis appearing to be central to these problems. The gut microbiota and the host organism maintain a constant delicate equilibrium under physiological conditions; this balance influences various health factors, including metabolism, nutrition, immune function, and disease prevention. Significant variations in microbiome makeup exist among healthy persons, and these variations may influence susceptibility to disease.

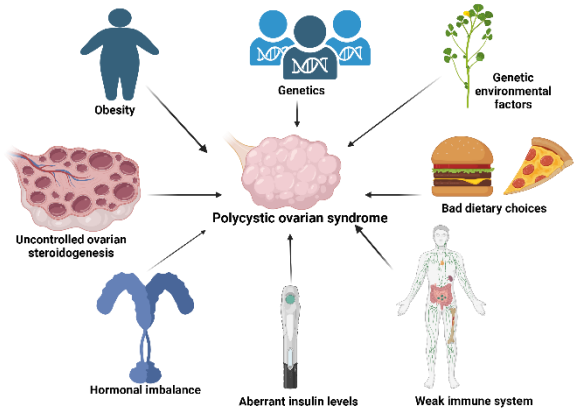

Fig.2: Causes of PCOS

Pathophysiology of PCOS

PCOS, also known as polycystic ovarian syndrome, is a condition that is distinguished by the presence of polycystic ovaries, high testosterone levels, and irregular menstruation cycles. The complex pathophysiological pathways that are the basis for polycystic ovarian syndrome (PCOS) are influenced by a number of factors, including hyperandrogenism, insulin resistance (IR), faulty steroidogenesis, and buildup of adipose tissue [9]. Within the HPO axis, the hypothalamic secretion of gonadotropin-releasing hormone (GnRH) is responsible for regulating both the generation of androgens and the resistance of the body to insulin. There is a possibility that an interference with the release of luteinizing hormone (LH) and follicle-stimulating hormone (FSH) could result in decreased levels of FSH and higher levels of LH simultaneously. Research has demonstrated that the combination of insulin and LH can result in an increase in the amount of androgens produced by follicular membrane cells. A further possibility is that an excessive amount of adrenocorticotropic hormone (ACTH) causes the adrenal cortex to create an excessive amount of androgens. Androgen levels that are very high interfere with the

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maturation of follicles, which in turn inhibits ovulation from occurring [10]. A lack of adequate research on the pathophysiological factors that contribute to polycystic ovarian syndrome (PCOS) continues to exist. According to the findings of recent research, the primary factors that contribute to female reproductive dysfunction include hyperandrogenemia, insulin resistance, and hyperinsulinemia. Polycystic ovary syndrome (PCOS) can be caused by inflammatory reactions and oxidative stress, both of which can have a negative impact on the quality of oocytes and the function of endothelial cells [11].

Diagnosis

Due to the fact that polycystic ovarian syndrome (PCOS) is one of those rare disorders that evades the most fundamental diagnostic instruments that are currently accessible, unfortunately, there is currently no procedure that can be considered completely reliable for diagnosing PCOS. In order to arrive at a differential diagnosis, it is necessary to examine the patient's symptoms and eliminate any disorders that could be considered potentially problematic [12]. To arrive at a differential diagnosis of polycystic ovarian syndrome (PCOS), it is necessary to eliminate the possibility of hyperprolactinemia, thyroid sickness, Cushing's syndrome, and adrenal hyperplasia. This can be accomplished by utilising the results of the tests that are associated with PCOS. In spite of the fact that it could be beneficial to take into consideration the patient's medical history, variations in weight, and signs of insulin resistance, the most typical tests consist of a pelvic examination, a transvaginal ultrasound, and a measurement of the hormone level[13]. Polycystic ovarian syndrome (PCOS) is a condition that can be identified by scans that show polycystic ovaries, high levels of androgenic hormones or symptoms, and irregular or infrequent periods, according to the National Health Service (NHS). In addition, the Rotterdam criteria are considered to be the gold standard for diagnosing PCOS in adults. It is necessary for an ultrasound to indicate either ovulatory failure, polycystic ovaries, or two incidences of clinical or biochemical hyperandrogenism in order to establish that a woman has polycystic ovarian syndrome (PCOS) [14].

II. NATURAL CHEMICAL CONSTITUENTS FOR PCOS PAIN MANAGEMENT

Polyphenols and flavonoids

Vegetables, fruits, grains, nuts, herbs, seeds, stems, and flowers from a wide variety of plant species contain significant quantities of hydroxylated polyphenols, which are more often referred to as flavonoids. There are a number of advantageous medical properties that they possess, such as antioxidant, anti-inflammatory, anti-cancer, anti-microbial, and neuroprotective activities[15]. Studies have shown that flavonoids have an anti-inflammatory effect because they stimulate antioxidant pathways in the body. Their ability to inhibit the release of arachidonic acid and enzymes like lysozymes and β-glucuronidase allows them to reduce the severity of inflammatory reactions[16]. Flavonoids, which include quercetin, genistein, apigenin, kaempferol, and epigallocatechin 3-gallate, have the ability to modulate the expression and activation of cytokines like interleukin-1beta (IL-1β), tumor necrosis factor-alpha (TNF-α), interleukin-6 (IL-6), and interleukin-8 (IL-8). Additionally, these flavonoids regulate the gene expression of numerous pro-inflammatory molecules, including nuclear factor kappa-light chain enhancer of activated B cells (NF-κB), activator protein-1 (AP-1), intercellular adhesion molecule-1 (ICAM), vascular cell adhesion molecule-1 (VCAM), and E-selectins. Furthermore, flavonoids inhibit inducible nitric oxide (NO) synthase, cyclooxygenase-2, and lipoxygenase, which are enzymes that contribute to inflammation[17].

Polyphenols have a regulatory function in immunity on account of the effects they have on gene expression, the control of immune cells, and the creation of cytokines that promote inflammation throughout the body. These substances have the ability to inhibit the nuclear factor kappa-light-chain enhancer of activated B cells, also known as NF-κB, and they also modify the pathways of arachidonic acid and mitogen-activated protein kinase (MAPk). Polyphenolic compounds inhibit the activities of a number of proteins that play a role in the regulation of protein synthesis. These proteins include phosphatidylinositide 3-kinases/protein kinase B (PI3K/AkT), IKK/JNK, mTORC1, JAK/STAT, and others[18]. In addition, they have the ability to prevent the synthesis of genes that are responsible for inflammation and the toll-like receptor (TLR). The anti-inflammatory actions that they have are accompanied by antioxidant activity and the ability to block enzymes that are responsible for the creation of eicosanoids. However, on the other hand, they inhibit enzymes such as xanthine oxidase and NADPH oxidase (NOX), which are involved in the generation of reactive oxygen species (ROS). Catalase, glutathione peroxidase (Px), and superoxide dismutase (SOD) are examples of natural antioxidant enzymes that are upregulated by these substances. Furthermore, they accomplish this by suppressing cyclooxygenase (COX), lipoxygenase (LOX), and phospholipase A2 (PLA2), which all contribute to the reduction of inflammation. As a consequence, this leads to a decrease in the production of prostaglandins (PGs) and leukotrienes (LTs). Certain physiologically active compounds have been shown to be able to ease the symptoms of a wide range of chronic inflammatory conditions, according to the available evidence[19].

Curcumin role in PCOS pain management

The management of polycystic ovarian syndrome (PCOS), which is a multi-factoral condition

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that is both complicated and diverse, is a challenging clinical problem due to the adverse consequences that it has on the reproductive health and metabolism of women[20]. Curcumin, a phenolic compound that has powerful antioxidant and anti-inflammatory activities, could be used in a viable therapy regimen for polycystic ovarian syndrome (PCOS). Furthermore, curcumin has the ability to improve insulin resistance and lipid profiles simultaneously. The naturally occurring polyphenol curcumin, which is sometimes referred to as differuloylmethane, is derived from the roots of the Curcuma longa plant, which belongs to the family Zingiberaceae[21]. Its origins as an Indian spice stretch back many years, and it has been used in a variety of applications, including as a spice, a colorant, and an additive. As a result of its anti-inflammatory, hypolipidemic, and anti-anxiety qualities, it is also utilized in the treatment of a wide variety of chronic illnesses, such as diabetes, depression, and anxiety[22]. According to an increasing body of data derived from scientific investigations, curcumin functions as a natural regulator and provides protection for the female reproductive process. In addition, it is regarded safe to use curcumin in high dosages (up to 12 grams in the human body) and for extended periods of time (up to four months). It should come as no surprise that curcumin safeguards ovarian tissue. This chemical has been shown to prevent ovarian fibrosis, promote matrix disintegration, and reduce the synthesis of vascular endothelial growth factor (VEFG), all of which are involved in the development of polycystic ovary syndrome (PCOS). There is evidence that this chemical promotes matrix disintegration[23].

A yellow tint is exhibited by the polyphenol curcumin. It is extracted from turmeric, which is a plant that is indigenous to the tropical region of Southeast Asia. Curcumin has been shown to have anti-inflammatory, anti-diabetic, and anti-obesity characteristics, according to recent research conducted on mouse models of obesity and diabetes. Curcumin has been shown to be effective in treating a variety of female reproductive disorders, including endometriosis, polycystic ovarian syndrome, and polycystic ovary syndrome those are just a few examples. In their study, Mohammadi and colleagues found that curcumin's antioxidant and anti-inflammatory benefits on polycystic ovarian syndrome (PCOS) could be attributed to its suppressive influence on the levels of tumor necrosis factor-alpha (TNF-α), serum interleukin-6 (IL-6), and C-reactive protein (CRP). Curcumin supplementation was found to improve blood insulin levels and the quantitative insulin sensitivity check index (QUICKI), according to the findings of a clinical study conducted by Sohaei and colleagues, which involved sixty different feminine participants[24]. An additional study found that women with polycystic ovary syndrome (PCOS) experienced improvements in their body weight, glycemic management, blood lipids (excluding triglycerides and very low-density lipoprotein, or VLDL) cholesterol levels, Peroxisome proliferated-activator receptor gamma (PPAR-γ), and low-density lipoprotein receptor (LDLR) gene expression after receiving curcumin therapy for a period of twelve weeks. Curcumin was able to reduce oxidative stress and the difficulties associated with cell death in people who were diagnosed with PCOS. Recent evaluations have focused on the impact that curcumin has on the lipid profiles of polycystic ovary syndrome (PCOS) and the management of glucose levels. Despite this, we conducted a literature review on the antioxidant effects of curcumin as well as its inherent mechanisms of action against the pathogenesis of polycystic ovary syndrome (PCOS)[25].

Resveratrol role in PCOS

Resveratrol, also known as trans-3,5,4'-trihydroxystilbene, is a polyphenol supplement that can be found in a variety of foods, such as grapes, berries, and nuts. There are a number of health benefits associated with it, including the reduction of inflammation, the prevention of cancer, and the maintenance of normal heart function. In recent years, there has been a lot of research that has been positive regarding the treatment of polycystic ovarian syndrome with resveratrol[26]. Resveratrol reduces testosterone production in rat theca-interstitial cells (T-I) by increasing the number of executioner caspases, reducing the number of viable cells, and limiting the generation of deoxyribonucleic acid (DNA), according to research conducted in vitro. Following administration of resveratrol, it was discovered that testosterone levels decreased in rats that were suffering from polycystic ovarian syndrome (PCOS), which is brought on by dehydroepiandrosterone (DHEA). The first clinical trial to assess the effects of resveratrol on polycystic ovary syndrome (PCOS) was carried out by Banaszewska et al., who found that patients with PCOS saw a significant reduction in the levels of androgens in their adrenal glands and ovaries. Due to the fact that resveratrol does not interfere with the capacity of the theca cells to make progesterone, its influence on the process of ovarian steroidogenesis is selective[27].

Mansour et al.,2021 was determined that the participants were females between the ages of 18 and 40 who had been diagnosed with polycystic ovary syndrome (PCOS) according to the Rotterdam criteria and whose monthly irregularities could not be explained by any other known cause. Over the course of three months, each person received either one thousand milligrams of resveratrol or one thousand milligrams of a placebo[28]. The random number assigned to each participant was one thousand milligrams. To determine which group would get resveratrol or placebo, 49 people were randomly assigned to one of the two groups. For the purpose of analyzing the outcomes, we utilized the intention-to-treat approach. According to the findings, women who were given resveratrol saw significantly

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lower rates of hair loss (32.10 percent versus 68.0 percent; p = 0.009) and a significantly higher rate of regular menstruation (76.47 percent against 51.61 percent; p = 0.03) than women who were given a placebo[29]. In addition, when we compared the lipid profiles of the two groups, as well as the levels of sex hormone binding globulin (SHBG), adrenal and ovarian androgens, and glycoinsulinemic metabolism, we did not find any statistically significant differences between the two groups[30]. In addition, the administration of resveratrol did not have any impact on the activities of the thyroid, liver, or kidneys[31]. The group that received resveratrol experienced a negative impact on body composition in comparison to the group that received a placebo; nevertheless, it did not bring about any changes in weight[32,33].

Quercetin role in the PCOS

Using quercetin, a chemical that is derived from Chinese medicinal herbs such as hawthorn, it is possible to effectively regulate insulin resistance in diabetics. When it comes to polycystic ovary syndrome, however, it is not apparent whether quercetin may or cannot diminish IR. A rat model of polycystic ovarian syndrome will be used in this study to understand the mechanism by which quercetin decreases insulin resistance[34]. The research will be conducted in order to accomplish this goal. To generate an in vitro model of polycystic ovary syndrome (PCOS), dehydroepiandrosterone was given subcutaneously into rats. We monitored the weight, menstrual cycle, and ovarian morphology of the rats before and after they were given quercetin. It was determined that the amounts of inflammatory cytokines in the serum could be determined through the use of an enzyme-linked immunosorbent assay. The expression of key genes that are involved in the inflammatory signalling system in ovarian tissues was determined through the use of Western blotting, real-time polymerase chain reaction, and immunohistochemistry. The nuclear translocation of nuclear factor κB (NF-AB) was also seen by the use of immunofluorescence[35]. In the insulin-resistant PCOS animal, the oestrous cycle would return 58.33% of the time after quercetin was administered to the animal who had the condition. There was a significant reduction in the levels of blood insulin, interleukin 1β, interleukin-6, and tumour necrosis factor α among individuals who consumed quercetin. The administration of quercetin in the rat model of insulin-resistant polycystic ovarian syndrome resulted in a significant reduction in the nuclear translocation of NF-κB from granulosa cells. Among the genes whose expression was inhibited by the treatment, ovarian tissue nicotinamide adenine dinucleotide phosphate oxidase subunit p22phox, oxidised low-density lipoprotein, and Toll-like receptor 4 were among those that were affected[36]. As a result of quercetin's ability to alleviate insulin resistance, the PCOS rats demonstrated a good therapeutic benefit. There is a possibility that quercetin's mechanism of action involves the inhibition of the Toll-like receptor/NF-κB signalling cascade, as well as the improvement of the inflammatory environment within the ovarian tissue of the PCOS human model[37,38].

Epigallocatechin gallate in PCOS

Polycystic ovarian syndrome (PCOS), which is the most frequent endocrine disorder in women of reproductive age, is characterised by inflammation of the ovarian tissue as well as oxidative stress. The anti-inflammatory and antioxidant characteristics of green tea extract (GTE) may give therapeutic benefits for the treatment of polycystic ovarian syndrome (PCOS)[39]. There are a number of benign health conditions that are prevalent among women in today's society, including endometriosis, uterine fibroids (UFs), adenomyosis, dysmenorrhea, and polycystic ovary syndrome (PCOS). There is a significant amount of agony and distress that these illnesses cause for the women who suffer from them, in addition to the fact that they induce infertility. The consequences of improving traditional treatment with naturally occurring chemicals, especially polyphenols, in addition to the surgical and pharmaceutical treatments that are already available are being investigated by researchers[40]. It is the catechin content of green tea that is responsible for the majority of the alleged health benefits that are associated with drinking green tea. There is some evidence to suggest that the chemical epigallocatechin gallate (EGCG), which is a naturally occurring substance that is not poisonous, may have anticancer benefits. Recent study has focused on its potential roles in cell division inhibition, apoptosis stimulation, and epigenetic control. While its antioxidant benefits are well-known, studies have also focused on its potential roles in these areas[41].

As a result of the fact that green tea accounts for twenty percent of the total tea supply, it is among the most widely consumed varieties of tea worldwide. In general, water is the liquid that is drunk the most[42]. Green tea contains catechins, which are phenolic chemicals that have various beneficial effects on human health. Catechins are natural antioxidants found in green tea. This is the reason why drinking green tea is so beneficial to your health. Green tea and its primary bioactive component, known as (−)-epigallocatechin-3-gallate (EGCG), have been shown to possess numerous advantageous health effects[43]. These include its high anti-oxidative properties, its ability to safeguard the bones and nervous system, its ability to combat cancer, its ability to reduce cholesterol levels, and its ability to prevent diabetes[44]. There has been a small amount of research conducted on the benefits of green tea on a variety of female reproductive issues, including polycystic ovary syndrome (PCOS), endometriosis, and dysmenorrheal[45].

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III. FATTY ACIDS AND LIPIDS ROLE IN PCOS PAIN MANAGEMENT

Omega 3 fatty acids

Patients diagnosed with polycystic ovary syndrome (PCOS) may discover that omega-3 polyunsaturated fatty acids (PUFAs) improve their health by reducing the likelihood that they may experience metabolic issues such as inflammation, insulin sensitivity, hyperinsulinemia, obesity, and abnormalities in their lipid profile[46]. In order to evaluate the current objective, a study was conducted for a duration of sixteen weeks. The purpose of this study was to investigate the impact of different sources of Ω-3 polyunsaturated fatty acids (PUFAs) on the digestibility of nutrients, weight gain, productivity (lipid profile, glucose, and insulin), reproductive profile (progesterone, follicle stimulating hormone (FSH), oestrogen, luteinizing hormone (LH), and prolactin), and histological examination of ovarian tissues in female Wistar rats[47].

Omega-3 polyunsaturated fatty acids, also known as n-3 PUFA, are a substance that can assist in the management of metabolic disorders, obesity, diabetes, and insulin resistance. In spite of the fact that numerous hypotheses have been proposed concerning the method in which n-3 polyunsaturated fatty acids (PUFA) positively affect health, very little is known about the particular proteins and pathways that these fatty acids regulate[48]. The dysfunction of mitochondria and the stress that is placed on the endoplasmic reticulum (ER) may be contributing factors in the development of insulin resistance[49]. It appeared that the formation of reactive oxygen species (ROS) and the accumulation of fat as a consequence of mitochondrial dysfunction were important mechanisms that led to cellular insulin resistance. Furthermore, the endoplasmic reticulum (ER) is physically and functionally related to mitochondria[50]. When the ER is stressed in instances of chronic overnutrition, the unfolded protein response is activated, which leads to the major inflammatory pathways that impair insulin action. According to one school of thinking, dietary lipids are one of the nutrients that have a key role in the development of insulin resistance[51]. It should be noted, however, that the impacts on the metabolic processes of cells are not consistent across all dietary lipids. According to the findings of several studies, the consumption of omega-3 polyunsaturated fatty acids (PUFA) in the diet has the potential to regulate mitochondrial bioenergetics and endoplasmic reticulum stress, hence reducing the development of insulin resistance[52,53].

Gamma linolenic acid role in hormone regulation

In addition to having an effect on a woman's capacity to conceive, polycystic ovarian syndrome (PCOS) is linked to metabolic problems such as inflammation and insulin resistance. PCOS is an endocrine condition. The inflammatory aspect of polycystic ovarian syndrome (PCOS) has been the subject of a large amount of controversy, which has been kicked off by numerous reports of high cytokine levels[54]. Gamma-linolenic acid (GLA) has been shown to be effective in reducing inflammation that is associated with a wide range of medical conditions. These conditions include atopic dermatitis, rheumatoid arthritis, obesity, vascular disease, and polycystic ovarian syndrome (PCOS). In order to investigate the expression of inflammatory cytokines in the ovary and peri-ovarian adipose tissue (POAT), this study makes use of a rat model of polycystic ovary syndrome (PCOS), which is caused by dehydroepiandrosterone (DHEA). In addition, the influence of γ-linolenic acid (GLA) on the cytokines that are present in POAT is also evaluated in this study[55]. An injection of 60 milligrammes per kilogramme of body weight of DHEA was given subcutaneously to female Wistar rats for a period of 28 days. After that, these rats with PCOS were administered GLA orally at a dose of 50 mg/kg for a period of fourteen days. An evaluation of the expression of cytokine genes was carried out using real-time PCR[56]. According to the findings, the DHEA group had a higher level of cytokine expression in both the ovary and the POAT. This suggests that ovarian adipose tissue may have a role in worsening the pro-inflammatory condition that is associated with polycystic ovary syndrome (PCOS). It is more significant to note that GLA was able to reduce the inflammation that is linked with polycystic ovary syndrome (PCOS) by reducing the expression of cytokines from the POAT in rats that had the condition that was caused by administering its injection[57].

Berberine improves insulin sensitivity

A number of medicinal herbs, including Hydrastis canadensis (also known as goldeneal), Cortex Phellodendri (also known as Huangbai), and Rhizoma Coptidis (also known as Huanglian), contain berberine, which is an alkaloid that is associated with the isoquinoline derivative. Due to the fact that it is both safe and affordable, it has gained widespread use due to the antibacterial characteristics that it possesses[58]. One of the many pharmacological activities that berberine has been shown to have, among many others, is the ability to inhibit chronic cocaine-induced sensitisation. Berberine has also been shown to have antibacterial, anticancer, anti-inflammatory, and blood glucose reducing properties. A new single-blind clinical observation found that taking dietary supplements that had certain natural elements, such as berberine, helped cure problems with lipid metabolism and lower cardiovascular risk factors[59]. Berberine was one of the natural compounds that was found in these supplements. On the other hand, there is a dearth of clinical evidence on the effect on weight loss. Berberine has been shown to prevent the differentiation of 3T3-L1 cells in vitro. Additionally, it has been shown to improve glycaemic management and

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reduce dyslipidaemia in clinical trials[60]. For the purpose of this study, the researchers wanted to determine the effects of administering berberine to individuals who were diagnosed with metabolic syndrome for a period of three months, as well as to preadipocytes that were extracted from human omental fat[61]. By administering 10 μM of berberine, we were able to demonstrate that the growth of human preadipocytes and the secretion of leptin and adiponectin were considerably reduced[62]. This inhibition was accompanied by a decrease in the expression of PPARγ2, C/EBPα, adiponectin, and leptin mRNA[63].

Piperine as anti inflammatory and pain relief activity

Natural sources of the alkaloid piperine can be found in plants belonging to the family Piperaceae. Some examples of plants that fall into this category include the long pepper (Piper longum L.) and the black pepper (Piper nigrum L.). Piperine, the primary fragrant ingredient that can be determined to be present in these plants, is isolated from the fruits of black pepper and long pepper[64]. According to Pei (1983), the percentage of piperine that can be found in these plants ranges from 1% to 99%. It is possible that it will assist the digestive system in functioning more effectively, and it possesses some anti-inflammatory effects. The use of plants as a reliable source of medicinal substances has been practiced by humans for thousands of years[65]. Research has shown that particular medicinal herbs have the ability to alter specific processes within the immune system, including both cellular and humoral functions. Several different types of plants that belong to the genus Piper are utilised in a variety of traditional medical practices. Within the family of peppers known as Piperaceae, the species Piper longum L., Piper nigrum L., and Piper galeatum L. are all members[66]. The three species are located in the tropics and subtropics, and their common names are "long pepper," "black pepper," and "helmet pepper" respectively. They are all found in the same region. According to sources, it is an essential component of Indian traditional medicine that is effective in treating a wide range of conditions, such as arthritic pain, gonorrhoea, menstrual cramps, tuberculosis, and infections of the respiratory tract[67].

Vitamin C for PCOS

Micronutrients, an example of which is vitamin C (sometimes referred to as ascorbic acid), are substances that the body requires in extremely minute quantities in order to ensure that cellular and tissue growth is carried out correctly. Vitamin C is easily lost in urine due to its solubility in water; therefore, it is essential to absorb it on a constant basis through the consumption of food[68]. Two examples of the antioxidant activities that vitamin C possesses are the scavenging of peroxyl radicals and the restoration of the antioxidant capacities of fat-soluble vitamin E. Similar to the effects of an antioxidant, the final product is a beneficial regulation of lipid peroxidation in both the plasma membrane and the intracellular space. Vitamin C's influence on the metabolic processes of the ovary in PCOS There was research conducted by Olaniyan and colleagues on Wistar rats[69]. The researchers discovered that the amounts of vitamin C are regulated during the menstrual cycle, and that vitamin C also controls the activity of the ovary and the menstrual cycle altogether. A decrease in vitamin C levels occurs shortly prior to ovulation, and then a subsequent increase occurs as the temperature rises following ovulation. The fact that all of this is occurring suggests that the ascorbic acid is being consumed during the pre-ovulatory phase, which ought to be beneficial to the process of ovulation. Ascorbic acid, which is found in high concentrations in the corpus luteum, is responsible for the increased production of progesterone and oxytocin through its effects. In addition, the presence of ascorbic acid in the ovaries may make it easier for the body to produce collagen, which is a protein that is necessary for the growth of the corpus luteum and follicles, as well as for the restoration of ovarian tissue after ovulation. In particular, ovarian cysts are a potential diagnosis in cases where these functions are impeded[70].

IV. POLYMERS USED IN PCOS MANAGEMENT

a. Biomaterials used in PCOS management

It has been reported that a variety of biomaterials, including hydrogels and scaffolds, have been utilised in the treatment of orthopaedic and cardiovascular-related medical conditions. Gynaecology, on the other hand, does not make much use of them[71]. Chitosan, collagen, alginate, hydrogels based on fibrin, and three-dimensional scaffolds are some of the biomaterials used in PCOS management[72]. The objective of this study is to demonstrate the value of these biomaterials for tissue engineering in the female reproductive system. It has been previously described that these biomaterials can be used to create a functionalised nano-drug delivery system that can execute tailored delivery[73]. On the other hand, there has been a paucity of study conducted on their potential as therapeutic agents, and this is particularly true in the context of polycystic ovary syndrome (PCOS)[74]. Because biomaterials in regenerative medicine have the potential to be used for a variety of purposes, including the treatment of polycystic ovary syndrome (PCOS), we have provided a concise summary of their significance below. In the beginning of the study, we talked about the factors that lead to polycystic ovarian syndrome (PCOS), as well as the shortcomings of the conventional medical approach to treating the affected disease[75].

b. Natural and semi synthetic polymers used in PCOS management

A wide variety of natural and synthetic polymers can serve as the basis for the development of biomaterials that are used in biomedicine and environmental research. Organic compounds are

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polymers that occur naturally in the environment. There are several different types of natural polymers, the most common of which are proteins such as collagen, silk, and fibrin; polysaccharides such as alginate and hyaluronic acid; and bacterial polyesters. Natural polymers have already found applications in a wide variety of diverse fields, including but not limited to wound healing, regenerative medicine, food packaging, drug delivery carriers, tissue engineering, stem cell morphogenesis, and many more. Synthetic polymers, such as poly(lactic acid), poly(acrylic acid), poly(vinyl alcohol), polyethylene glycol, and many others, have a wide range of applications. Some of these applications include controlled drug release systems, tissue engineering, dispersion of bacterial biofilms, gene delivery systems, bio-ink in 3D printing, textiles in medicine, agriculture, heavy metals removal, and food packaging. Both biocompatible and biodegradable properties are possessed by these polymers[76].

V. CONCLUSION

Polycystic ovarian syndrome (PCOS) is on the rise among reproductive-aged women and is a difficult condition with long-term repercussions. Imprecise diagnostic criteria and the immense intricacy of this syndrome's traits are the most difficult parts of dealing with it. The timely implementation of individualised treatment choices has the potential to enhance the treatment of polycystic ovary syndrome (PCOS), decrease the number of comorbidities, and enhance the quality of life. Women who are in their reproductive years and may experience infertility should be evaluated and treated as soon as possible in order to improve their chances of having a fertile child. The identification of significant gene polymorphisms has the potential to be of assistance in the early screening and diagnosis of PCOS subtypes. Among the many pathological characteristics of polycystic ovary syndrome, the natural molecules that are being described here include a wide range of chemical components that have an effect on ovarian function, metabolic profile, inflammation, oxidative stress, and hormonal and metabolic abnormalities. Piperine, resveratrol, flavonoids, vitamins (particularly vitamin C), omega-3 fatty acids, and polymers that are either made or occur naturally are some of the naturally occurring substances that are included in this category. It appeared that omega-3 fatty acids were able to improve the symptoms of polycystic ovarian syndrome in women who were over 20 years old. On the other hand, close monitoring is necessary because there is a possibility of adverse effects and interactions with particular pharmaceutical treatments.

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