Journal of Biochemistry and Biophysics

(A PEER-REVIEWED AND REFEREED JOURNAL)

Volume 9 Number 1 January - June 2024

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JOURNAL OF BIOCHEMISTRY AND BIOPHYSICS

JANUARY – JUNE 2024
VOLUME 9, NUMBER 1

e-ISSN - 2582-3442
p-ISSN - 2582-3558

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Review Article

Journal of Biochemistry and Biophysics
Volume 9 Number 1, January - June 2024
DOI: http://dx.doi.org/10.21088/rfpjbb.2582-3558.9124.1

Review of Biochemistry of Dopamine and it's Biological Significance

Alpana Saha

How to cite this article:

Alpana Saha, Review of Biochemistry of Dopamine and it's Biological Significance. RFP Jour. of Bio. and Biophy. 2024;9(1): 075–078.

Abstract

The chemical formula of dopamine is $C_6H_3(OH)_2$-CH_2-CH_2-NH_2. Normally dopamine is abbreviated as DA, that is, dopamine (DA). There are many chemicals in the category of cathecolamine and dopamine is one among them. Dopamine plays crucial role in the life of human beings and many other animals. Dopamine is essential for feel good factors in humans and many other mammals. They deficiency of dopamine stimuli or secretion in brain can lead to many mental diseases.

Keywords: Amino acid, Cathecolamine, Deficiency, Dopamine, Mental disease.

INTRODUCTION

In every living being cell-to-cell communication is very important for healthy survival. The communication process among cells is called transduction. Dopamine is a neurotransmitter that helps in transduction and chemically is a monoamine catecholamine and a hormone that carries out many functions. It is definitely made in our brain. Being a neurotransmitter the role of dopamine in our brain is to help us in movement, memory, mood control, sleep, attention, motivation, pleasure reward, arousal, behaviour and cognition.

High or low secretion level leads to many neuromotor diseases in humans. Some of the common such diseases are hyperactivity disorder, restless leg and Parkinson's disease.

Most of the addictive chemical leads to secretion of high dose of dopamine hormone in our body and brain. This high dose gives us great sense of satisfaction and pleasure. On the contrary low secretion of dopamine in the body leads to mood swings, unhappy state, being unmotivated and tired. So optimum amount or a balance amount of dopamine secretion is required in the body to remain focused, alert, motivated and happy.

High level of dopamine also leads to problems like addiction, mania and obesity. Imbalance level of dopamine secretion in the brain leads to mental disorders like Schizophrenia. This is because of high secretion of dopamine in certain regions of the brain and low secretion in certain other.

Sometimes this question is generally asked how do dopamine impacts a drug addicts?

Addictive drug or recreational drugs interfere with the nervous system of our body. If taken continuously addictive drugs weakens the nervous

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Received: 11.11.2024 **Accepted:** 12.12.2024

system impacting the response one gets with reward signal usually when with some dopamine stimulus. To achieve the same the addicts continuously depend on the dose of drug they are edited to a regular interval to get that kick.

Therefore, dopamine is not directly involved in drug users surge in behaviour. But dopamine secretionis such designed after addiction that it gives the urge of going back to the drug intact after a fixed time and to get the desired reward of pleasure.

There certain food that contains high magnesium dose and it is said magnesium is important for appropriate dopamine secretion in the body. So, we need to take good food and nutrients to avoid lack of dopamine secretion in the body. Good intake of almond, green leafy vegetables, banana, beetroots, oranges and green tea are good for dopamine level in the body.

OBJECTIVE OF THE STUDY

Objective of the study is to know the structure of dopamine and various physiological and psychiatric disorder associated with dopamine malfunctioning.

LITERATURE REVIEW

Dopaminergic system is important for mental health of the human body. Many pathological conditionslike Schizophenia, Parkinson disease etc take place because of the disfunctional dopamergic transmission in the body. Dopamine receptors help to overcome hallucination and delusion caused during schizophrenia. Dopamine deregulation in the body causes serious help issues in the human body and brain. One of the challenges of scientists, pharma, medical experts and doctors have to find dopamergic drug which has no adverse effect. A great achievement in the field of dopamine research surfaces a decade ago.[5]

The neurotransmitter is involved in behaviours like food craving, decision making and various executive functions of human beings. Some human beings show the symptom of binge eating, which is also connected with the dopamine regulation deviation in the body.[6]

We very well know that the neurotransmitters are very well with the help of neural transmitters or neural signals from the central and peripheral nervous system. Dopamine is an important neurotransmitter of central nervous system that function in the most of the activities of human behaviour.[7,8]

Dopamine is synthesized by the precursors of kidney and the brain area of an animal body specifically in humans. The importance of dopamine in human brain lies in its role in the sense of pleasure with the work a human beings do in its day-to-day life. Motor control in humans and lactation in feeding females are all the result of proper functioning of dopamine neurotransmitter.[9]

Discussion the Structure of Dopamine

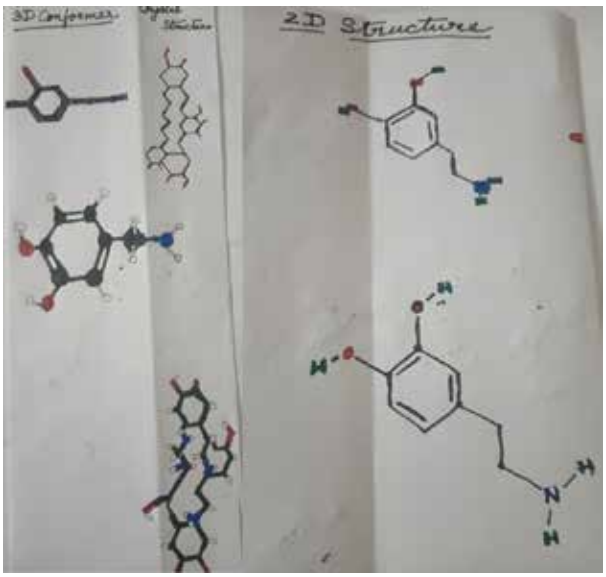

Fig. 1: 2D, 3D and crystal structure of dopamine

Dopamine's chemical structure is $C_8H_{11}NO_2$ and it is a chemical of catechol family and called catecholamine (*Fig. 1*). Catechol is the family in which position 4 hydrogen is substituted with 2-aminoethyl group.

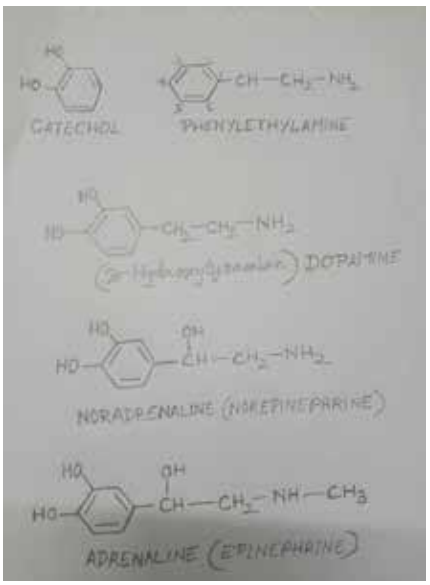

Fig. 2: Structures of main catecholamines

Only dopamine is not the hormone belong to the catechol family but adrenaline (epinephrine) and noradrenaline (norepinephrine) also belong to this family. These are the hormone secreted from adrenal gland (*Fig. 2*).

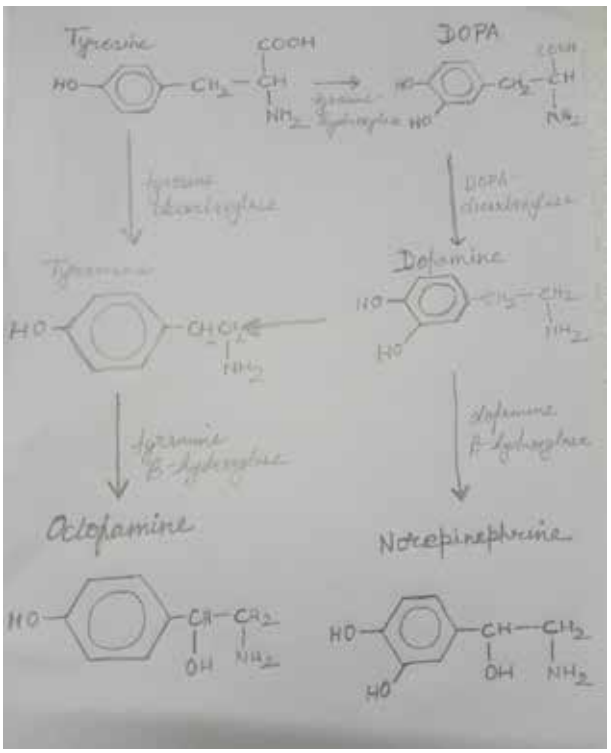

Fig. 3: Representation of biosynthetic pathways and chemical relationships

Fig. 3 represent the biosynthetic pathways and chemical relationships between all the neurotransmitter hormones and enzymes involved in these pathways. Octopamine, norepinephrine, dopamine, and tyramine are all synthesized by tyrosine.

Most of the moving animals are found to have behavioural pattern impacted via neurotransmitters. In mammals body motions are dependent on dopamine. Most of their locomotory action depends on dopamine. In search of food reward animals move from one place to other as much as they can. Some of the experiments have shown that mammals have reflect strong response to dopamine both for primary rewards like food and water and temporary rewards like motivation etc.[1-3]

In diseases like Parkinson's disease (PD) is loss of nigral dopaminergic neurons.

Anomalous motor behaviour has been shown to robustly correlate with measures of communicative function, suggesting an involvement of the physiology and psychological studies. The nanomaterials are metals, metal oxides, electrodes, cathodes, anodes, polymers, carbon oxides etc. Electromagnetic material or in other words electronic devices made of nanomaterials help in easy detection of function of neurotransmitters like

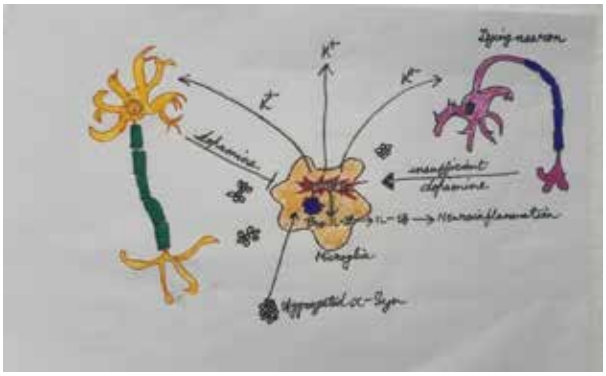

Fig. 4: A sketch diagram of dopamine in Parkinson's disease

sensorimotor system in impaired communication. At the neural level this is supported by the evidence that communicative and motor behaviours have all been linked to different areas within the basal ganglia via a series of parallel (yet overlapping) projections from and to frontal cortical regions.[4]

DISCUSSION

A diseased condition called binge eating disorder (BED) and bulimia nervosa (BN) is characterised by eating in huge amount uncontrollably. Enhanced food craving and decreased decision-making capacity are some of the effects of this diseased caused to the human body.[7]

Hedonic hunger is associated with the sense of lack of energy and people start eating uncontrollably to attain a desired level of pleasure of eating. Such situation leads to other health hazards condition like overweight, obesity and life style diseases associated with weight gain.

In human body termination of dopamine function occurs because of clearance of dopamine singling in the body. This can be impacted by many chemicals, physical and physicalistic conditions.

The detection of dopamine in real behaviour in human is very important area of research. Electronic or electromagnetic biosensors are used to detect function of dopamine, dopamine regulation on human behaviour. Nanomaterial modified materials electronic devices are used to detect dopamine regulation and receptions in human and animal bodies to study its effect on behaviour,

dopamine in the human or animal bodies.[8]

Generally, dopamine is stored in the adrenal gland and dopaminergic vesicles. Dopamine is also an important neurotransmitter not only for brain but also for eye and retina. According to IUPAC (International Union of Pure and Applied Chemistry that names the chemicalmolecules), the name (ID) of dopamine is as follows: IUPAC ID: 4-(2-aminoethyl) benzene-1,2-diol[9]

CONCLUSION

The study has helped us conclude that the development of new DNA recombinant technology has helped us easily identify DNA receptors subtypes. The technology of use of targeted mutagenic agent helps us identify ligand of receptor dopamine. Presently with all available DNA technologies we are able to identify dopamine receptors area and its function in the brain areas. The structural details and receptor areas of dopamine has been explained in this study. Even the potential function of each receptor sites of dopamine has also been discussed at large in this study article. Even the disease cause both with the hypo and hyper secretion and receptor malfunction has been mentioned in this study. Behavioural studies show that human behaviour is very well dependant on dopamine secretion.

Through our study we have also found out that dopamine has been also involved in the food behaviour of human beings. Binge eating is a symptom of a nervous disease called bulimia nervosa which is generally connected with other serious health issues. In these patients, suffer from strong desire of food at certain trigger situation when they find themselves lacking dopamine spike in the body and the body crave for the same. However, the exact physiological marker to define binge eating is still lacking among the scientists.

Almost all studies in our review of studies have indicated the role of dopamine level, regulation of dopamine and its receptor in the behaviour of human being related to psychiatric condition and behaviour work.

Conclusively we can definitely say that dopamine is an amino acid that brings happiness.

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Review Article

Journal of Biochemistry and Biophysics
Volume 9 Number 1, January - June 2024
DOI: http://dx.doi.org/10.21088/rfpjbb.2582-3558.9124.2

Sickle Cell Disease: A Review Study

Abhishweta Saxena[1], Sachin Narwadiya[2]

How to cite this article:

Abhishweta Saxena, Sachin Narwadiya, Sickle Cell Disease: A Review Study. RFP Jour. of Bio. and Biophy. 2024;9(1): 079–082.

Abstract

Sickle Cell Disease (SCD) is a hemoglobin disorder that requires lifelong management and contributes to infant, childhood as well as adult morbidity and mortality. SCD is a widespread disease characterized by a variation in the beta-globin gene that results into the production of aberrant hemoglobin called hemoglobin S. The inheritance of the mutation could be homozygous or heterozygous combined with another hemoglobin mutation. SCD can be identified by the presence of dense, sickled cells that grounds for haemolysis of blood cells, chronic anemia, acute painful occurrence, body part alteration, and in many cases death. Early detection/diagnosis of SCD can help to reduce the mortality and management of the disease effectively. Millions of people worldwide are impacted by this prevalent inherited blood disorders, which include sickle cell disease and its variations. Sickle Cell disease results in a markedly reduced life expectancy, particularly in India's tribal people. The review study here explain an overview of the inheritance, severity, pathogenesis, present-day and emergent techniques for SCD detection and highlights the different national & International programs for the elimination of disease from the population.

Keywords: Sickle cell anemia; SCD; Hemoglobinopathies; Detection; Diagnosis; Point of care; National Program; Elimination.

INTRODUCTION

Blood is a special fluid in the body that consists of four main components: plasma, red blood cells, white blood cells and platelets. Hemoglobin (Hb) is a protein molecule found in red blood cells (RBCs) that carry oxygen and provide red blood throughout our body. Normal red blood cells are biconcave, have no nucleus, and are flexible, which helps them move easily through the smallest blood vessels called capillaries. Sickle cell disease is a red blood cell disease caused by a genetic mutation that causes atypical hemoglobin production. This causes red blood cells to lose their normal shape, take on a C shape like a virus or crescent, and fall off easily. These tough, sticky cells can get stuck in small blood vessels and block them, slowing or blocking the flow of blood and oxygen to some parts of the body. It is one of the most common monogenic diseases worldwide with autosomal recessive inheritance (Rees, DC 2010).

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Received: 18.06.2024 **Accepted:** 20.12.2024

Sickle cell syndrome is common and affects 70% of births worldwide. Sickle cell disease (SCD) is a genetic disease caused by mutations in the gene encoding hemoglobin beta subunit (HBB) that can lead to sickle cell anemia (SCA), HbSC, or HbSβ-thalassemia (Kato GJ, 2018). Public health in India is a major challenge, especially for tribal people (Colah RB, 2015). SCD is characterized as a somatic chromosomal disorder. Hemoglobin (HbS) allele βS is a hemoglobin subunit β allele in which an adenine-thymine mutation in the sixth codon of β-globin leads to glutamate substitution at position 6 in the β-globin chain with Amino acid replacement to valerin. . Although caused by changes in context, its symptoms are also influenced by behavior and environment (Rees DC, 2022). It is a chronic disease that varies in severity and requires lifelong treatment (Brousse V, 2014). (Under 5 years of age) Sickle cell anemia ranks 12th among all causes of death. The highest burden of SCD is reported in Western and Sub-Saharan Africa and India (GBD 2021 Sickle Cell Disease Collaboratives, 2023). SCD is more common across ethnic groups, with a prevalence of 40-55% (Colah RB, 2015). SCD is one of the top ten diseases faced by people in India. However, birth rates in India have fallen from 21% in 2000 to 16% in 2021 (GBD 2021 Sickle Cell Disease Collaboratives, 2023). High risk increases morbidity and mortality in infants and children; Approximately 50-90% of children born with type 2 diabetes die before the age of five (Gyamfi J, 2019). Although influenza is resistant to malaria. This review discusses the etiology and epidemiology of cell disease, its course, major problems, treatment, and future research on the disease.

Sickle Cell Disease: Pathophysiology Normal red blood cells can survive up to 120 days, but sickle cells can only survive 10 to 20 days. The main pathophysiology is based on the polymerization of deoxygenated HbS and the formation of long fibers in erythrocytes, which causes erythrocyte distortion, resulting in strong hemolysis and vascular occlusion. Additionally, infected cells are destroyed by the spleen due to their shape and hardness. Sickle cells accumulate in these filters and die. When there are fewer healthy red blood cells in the body, a person can become anemic and diseased cells can damage the spleen. Sickle cell anemia causes many problems such as active disease, pain and inflammation in the brain, liver, lungs, etc. It can cause damage to many parts of the body, including (Bunn HF. 1997). Types of Sickle Cell Disease Most human hemoglobin A (HbA), also known as adult hemoglobin (hemoglobin A1 or α2β2), consists of two beta globin subunits and two alpha globin subunits. These two genes must function properly and work together to produce normal hemoglobin for human children and adults. When hemoglobin is not properly replaced with normal hemoglobin (HbA), a person may become sick or ill. If normal heme (HbA) is replaced by abnormal hemoglobin, the person may become sick or ill. Sickle hemoglobin (HbS) is the result of mutations in the β-globin chain. If only one beta globin subunit is affected, the person has a good thing, and if both are affected, the person has sickle cell disease. Patients with cancer inherit HbS from one parent and HbA from the other parent, making them heterozygous and causing the disease. People with cancer inherit two HbS genes from their parents, making them homozygous. Sometimes a person can get the beta thalassemia gene from one parent and the cancer gene from the other parent.). This is often called sickle cell anemia/disease and is usually the most severe form of the disease. One parent and one gene for beta thalassemia (another type of hemoglobinopathy). People with HbS beta thalassemia often have severe SCD.

EPIDEMIOLOGY

Sickle cell trait (SCT) is more common in people of African descent and in people whose ancestors came from tropical and subtropical regions where malaria is common. In the United States, 0.2% of whites and 9% of African Americans have breast cancer (Gibson JS, 2016). Approximately 300 million people worldwide have this disease, with sub-Saharan Africa accounting for one-third of this number (El Ariss AB, 2016). Sickle cell trait is more common in areas where malaria is common. According to a study, the prevalence of SCT can reach 25% in some African countries and 60% in Saudi Arabia. SCT and disease prevalence are likely to increase in the western part of the world due to large migration of people from high disease burden regions such as Africa and the Middle East (Rogers ZR, 2023). Many people have been examined in India and according to various studies, the states where SCD is found are: Gujarat, Rajasthan, Uttarakhand, Maharashtra, Bihar, Jharkhand, Madhya Pradesh, Chhattisgarh, Odisha, West Bengal, Tamil Nadu, Telangana, Andhra Pradesh, Karnataka, Kerala. States, Uttar Pradesh and Assam. The HbS allele frequency varies between 0.011 and 0.120, the β-thalassemia allele frequency varies between 0.005 and 0.024, and approximately 26.2% is associated with iron deficiency. (Information from Ministry of Tribal Affairs). (ACS), aseptic necrosis of bones, microinfections in the spleen,

brain and kidneys, disease, paralysis and physical damage to various organs of the body. Recent research reiterates that individuals with SCD may experience red blood cell dehydration, abnormal migration of red blood cells to the vascular endothelium, inflammatory events, and depletion of all cells in blood vessels, and abnormal nitric oxide metabolism can cause thrombotic problems and various diseases. Other problems, such as infections and hand-foot syndrome (dactylitis), occur as swelling of the hands and feet. Given the effect of infection on the spleen, the immune system of people with this disease may also be affected. Therefore, people with SCD have weak immune systems and are more prone to infections (El Ariss AB, 2016). Technologies commonly used for SCD diagnosis include high-performance liquid chromatography (HPLC), isoelectric focusing (IEF), and capillary electrophoresis (CZE). Cell Tests A complete blood count (CBC) is the first test used to diagnose various types of diabetes. However, heme mutations can affect hematological parameters (Greene, D.N, 2014). Peripheral blood smear (PBF) is usually performed after detecting an abnormality in the automated count and is considered an important part of the hematological evaluation. PBF examines the morphology of blood cells and evaluates any changes; this can provide important information to help identify different types of diabetes (Nwogoh, B, 1974). Another important diagnostic test is the solubility test based on HbS polymerization in the deoxygenated state. The solubility test of its content, now most used, is based on Hb-S inequality in the presence of concentrated phosphate buffer, hemolytic reagents and sodium dithionate. Electrophoresis is a chromatographic technique that is considered one of the main tests for testing Hb variants (Wajcman, H, 2011). Different pH values and environments are used to identify hemoglobin; for example, cellulose acetate electrophoresis at alkaline pH or citrate agar at acidic pH (Kotila, T, 2011). The preferred technique for this purpose is capillary electrophoresis and has been shown to separate the Hb fraction and diagnose sickle cell disease and thalassemia. Isoelectric focusing (IEF) is a high-resolution technique used to separate proteins based on their isoelectric point (pI). Hb molecules move along the pH gradient until they reach the isoelectric point where the charge is zero. Hb molecules precipitate and appear as sharp bands (Reddy, M.N, 1994). As a previous technology, HPLC has been shown to be able to separate hemoglobin due to its different interactions with the stationary phase. HPLC detects different types of heme depending on retention time and image pressure. Each hemoglobin has a specific retention time that is comparable to the retention time of known heme products. HPLC is less sensitive and reliable in monitoring patients receiving serum or hydroxyurea (Gupta, P.K, 2009).

Sickle Cell Disease: Treatment/Removal There are three main treatment methods that change the disease, such as the use of hydroxyurea, red blood cell transplantation and hematopoietic stem cell transplantation (Ka Kassim AA, 2014). There is no treatment other than stem cell transplantation. Although there is no permanent cure, early diagnosis or universal screening remains the key to better control of the disease. Four overlapping testing phases (antenatal, perinatal, neonatal, and postneonatal) are required for effective disease management. Prenatal screening can help detect SCD ininfants with previous symptoms early in life, before birth or in the first few days of life (Arishi WA, 2021). The severity and impact of the disease varies greatly, with proper management can reduce problems, improve the lives of those affected, and improve their quality of life. The best strategy to reduce this disease is genetic education including prenatal and pregnancy counseling and information to avoid pregnancy with a child with homozygous genotype. The severity of the disease in the group is still controversial. The Government of India (GoI) and the Ministry of Tribal Affairs (MoTA) have set a target to eliminate SCD. Newborn screening is important to reduce morbidity and mortality by promoting early diagnosis and preventive treatment for individuals seeking health and harmony by the National Mission to Eliminate Sickle Cell Anemia by 2023.

Funding: This research received no external funding.

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: Not applicable.

Conflicts of Interest: The author declares no conflict of interest.

CONCLUSION

There is currently no way to permanently cure this disease. However, with appropriate treatment, the severity and severity of the disease can be controlled, thereby improving the quality of life and life expectancy of the patient. This can be managed effectively by services providing medical treatment with genetic testing and counselling.

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Review Article

Journal of Biochemistry and Biophysics
Volume 9 Number 1, January - June 2024
DOI: http://dx.doi.org/10.21088/rfpjbb.2582-3558.9124.3

A Comprehensive Review on Antimicrobial Efficacy of an Essential Oil 'Eugenol'

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How to cite this article:

Sushma T, Madhusudhan MC, Jameel NM, *et al.,* A Comprehensive Review on Antimicrobial Efficacy of an Essential Oil 'Eugenol'. of Bio. and Biophy. 2024;9(1): 083–090.

Abstract

The increasing need for effective antimicrobial agents has become paramount due to the rising prevalence of antibiotic resistance among pathogens. In the current scenario, the overuse and misuse of antibiotics in clinical and agricultural settings have accelerated the development of resistant strains, creating an urgent demand for alternative therapies. Antibiosis, the mechanism by which antibiotics exert their effects, primarily involves inhibiting cell wall synthesis, disrupting protein production, or interfering with nucleic acid replication. While synthetic antibiotics have dominated the market, there is growing interest in natural sources of antibiotics, particularly plant-derived compounds. One such compound, eugenol, found in essential oils, has shown promising antimicrobial properties. Eugenol not only inhibits various foodborne pathogens but also enhances the efficacy of conventional antibiotics by lowering their minimum inhibitory concentration (MIC), making it a valuable candidate for use in combination therapies.

Keywords: Antibiosis; Antimicrobial resistance; Bioactivity; Essential oil; Eugenol.

INTRODUCTION

One of the main methods to improve beneficial biological effects and minimize potential adverse effects is to modify the molecular structures of naturally occurring physiologically active chemicals.[1] According to estimates from 1998, 60% of anticancer and anti-infective medications on the market or in clinical trials came from natural sources through structural alterations.[2] More recent data from December 2014 reveal that 138 (or roughly 58.30%) of the 237 anti-infectious agents (antibacterial, antifungal, parasitic, and antiviral) recognized by public health agencies globally, are natural products or products derived from natural products. Therefore, it is obvious that this is a field of study with excellent promise for discovering new medicines.[3] Eugenol was initially discovered in 1929 and commercial manufacturing of the natural chemical, which is utilized as a target

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Received: 10.09.2024 **Accepted:** 13.11.2024

molecule for the creation of bioactive compounds, started in the United States in 1940. Although it can be made synthetically, *Ocimum tenuiflorum, Cassia fistula, Zieria smithii,* and *Pimenta racemosa* are the primary sources from which it is harvested. Eugenol is light-yellow oil with a spicy flavor and a clove-like aroma, an allyl-phenol type phenyl propanoid. It has an extensive applications in the pharmaceutical, food, agricultural and cosmetics industries[4] and when tested against the fungi Cladosporium spp.[5] it shown potential antibacterial and antioxidant activities.[6] Other actions, such as antiviral, anti-inflammatory and inhibitor of platelet aggregation, have been documented in the literature. Additionally, it qualifies as a key provider of leishmanicidal due to its anti-Leishmania efficacy and minimal cytotoxicity.[7] Eugenol is a target molecule for structural changes to generate substances with medicinal properties because of its wide range of biological action.

Currently, bacterial infections and cellular oxidation stand out among the different clinical diseases, both of which have significant effects on public health. Commercial antibiotics are frequently unable to stop bacterial growth due to the resistance development and mutation mechanisms in microbes, leading to failures in the treatment of multi-resistant bacteria. Consequently, bacterial resistance has emerged as a global public health issue.[8] Aerobic organisms have the capacity to generate free radicals, which when in excess can start a cascade of reactions that harm or kill cells. Therefore, many illnesses develop, including cardiovascular and neurological conditions. The application of antioxidants in diet has proven to exhibit a substantial impact on the prevention of various diseases in the battle against the damage caused by the generation of free radicals.[7] According to reports in the literature, eugenol reduces oxidative stress and has positive benefits on health.

Eugenol has diverse biological activities, the current review focuses mainly on the antimicrobial effects.

Antimicrobial activity

There are numerous natural, semi-synthetic, and artificial substances that have the potential to significantly alter metabolic and physiological processes. These substances include lactams and glycopeptides that alter the synthesis of cell walls, tetracyclines and macrolides that inhibit protein synthesis, sulphonamides that block the functions of certain metabolic pathways, and fluoroquinolones that disrupt DNA replication and translation.[9-10] Healthcare organizations are significantly concerned about bacterial resistance. The likelihood that bacteria will develop more complex resistance to antibiotics increases with increased global use of antibiotics. Because of this, some new modified strains seem to have decreased the likelihood that the treatments will be properly effective in patients, having serious repercussions that can lead to morbidity and mortality or clinical complications.[11] The ineffectiveness of the usage of antibiotics in healthcare is hampered by bacterial resistance, and there is strong evidence that improper use of antibiotics will ultimately lead to the development of resistance.[11] Additionally, the risk of managing immunity-compromised health conditions like cancer, HIV infection, surgery, and diabetes is reduced due to the lack of adequate access to effective antibiotics.[12] Although this is considered a natural process, there is a lack of information regarding the crisis of antibiotic resistance, accelerated by passive human activities such as inappropriate prescription practices, misuse of antibiotics by both physicians and patients, and incorrect diagnoses has significantly increased the rate of antimicrobial resistance.[13-14]

Mechanisms for antimicrobial activity

Understanding the modes of action of antimicrobial medications is crucial to understanding the processes of resistance. Antimicrobial agents concentrate on particular significant bacterial functions. Different antimicrobial agent classes kill or inhibit bacteria in different ways. It can categorize the different ways that antimicrobial agents function into the following groups.

Preventing the cell wall from being produced

It is essential for preserving the shape of the bacterial cell and protecting the bacteria from lysis caused by the high intracellular osmotic pressure is crucial, due to the elastic macromolecule that constitutes the bacterial cell wall.[15,16] Peptidoglycan is the primary component of the bacterial cell wall, consists of long glycan chains made of N-acetylglucosamine (GlcNAc) and N-acetylmuramic acid (MurNAc), which are cross-linked by short peptides (composed of four amino acids). This cross-linking is facilitated by enzymes known as transpeptidase and carboxypeptidase, collectively referred to as "Penicillin-Binding Proteins." Many antibiotics, including -lactam and glycopeptides, focus primarily on this physical

barrier.[16] Antibacterial drugs include the lactams (penicillin's, cephalosporins, carbapenems, and monobactams) and the glycopeptides (vancomycin and teicoplanin), which prevent the growth of bacterial cell walls.[17]

Preventing the synthesis of protein

Antibiotics that stop protein synthesis are essential for bacterial growth and development. When protein synthesis is suppressed, cell proliferation is either halted or slowed down.[18]

Tetracyclines, macrolides, and aminoglycosides were preventing the synthesis of new proteins by attaching to the 30S subunit and some of the antimicrobials can cause an error in protein synthesis.[19]

Preventing the synthesis of genomic material

Broad-spectrum antibiotics known as fluoroquinolones are used to treat gram-positive, gram-negative, and anaerobic bacteria. In gram-negative bacteria, fluoroquinolones act as inhibitors of the DNA gyrase enzyme, which is essential for the start of DNA replication, and in gram-positive bacteria, as an inhibitor for the topoisomerase IV enzyme, which is essential for daughter-cell segregation (decatenation).[20-21] Quinolone antibiotics work to inhibit DNA supercoiling by interacting with either topoisomerase IV or II. which results in double-stranded DNA breaking down and cell death. Either using a method that depends on protein synthesis or one that doesn't.[22]

Inhibition of bacterial enzymes or metabolic pathways

The folate biosynthetic pathway is an excellent target for antibiotics because eukaryotic cells acquire folate through an active transport system, whereas microorganisms must synthesize it de novo. To synthesize folate, the enzyme dihydropteroate synthase (DHPS) requires para-aminobenzoic acid (PABA). Sulphonamides have been observed to prevent the application of para-aminobenzoic acid (PABA) in bacterial folate synthesis.[23] Sulphonamides share structural similarities with PABA and act as a substitute substrate for PABA as a competing inhibitor to stop the growth of bacteria by consuming the folate pool.[13] The final enzyme in the sequence, dihydrofolate reductase (DHFR), has served as a target for dihydrofolate pyrimidine antibiotics, like trimethoprim.[24-25]

Alteration to the bacterial membrane's structure

The Polymyxin molecules bind to the cell membrane of bacterial peptidoglycan and change the structure of the membrane to make it more permeable. These modifications cause an osmotic imbalance that results in the expulsion of cellular compounds, the inhibition of respiration, and quick water absorption that results in cell death.

Antimicrobial Resistance (AMR)

Historically, it is well established that, humans have fought a protracted battle with microorganisms, particularly bacteria, which has resulted in substantial morbidity and mortality in various human populations all over the world. Penicillin was a powerful antimicrobial agent for bacteria in the early 1940s. Consequently, it was widely used by people to combat numerous infectious diseases. Penicillin's efficacy has decreased due to overuse, though, as bacteria have begun to develop a number of resistance mechanisms.[18] The capacity of microorganisms to persist and be viable in the existence of antimicrobial agents is known as antimicrobial resistance (AMR). AMR has been developed within the bacteria as a result of prolonged and intensive use of antibiotics over time. The natural genetic evolution of bacteria to resist antibiotics has reached paradoxical heights in the twenty-first century, and this has made AMR a serious health threat with potential global repercussions that calls for immediate action. There are multiple ways in which they develop resistance are by intrinsic/acquired resistance, acquired itself contains alternative methods to develop resistivity through enzyme modification or inactivation of microbicidal molecules inside the cells and also by altering the target site for binding can further impact their efficacy.[9]

Kinds of antimicrobial resistance

Intrinsic Resistance: Some particular bacterial genera (or species) have distinctive structural/ functional traits that give them antibiotic resistance. These bacterial populations often lack a target site for the specific antibiotic, making it ineffective. For instance, Mycoplasma species are resistant to glycopeptides and lactam antibiotics because they lack a cell wall. Additionally, the presence of an outer membrane hinders the entry of antibiotics into bacterial cells. Further, this resistance may be due to the presence of an export system (such as the AcrAB-TolC system) or the ability of certain bacterial species to produce enzymes that inactivate antibiotics, such as the AmpC β-lactamase in E. coli.[26] Acquired Resistance: In this situation, naturally susceptible bacteria can become resistant to some antibiotics by acquiring their

genetic material from other bacterial strains. The three primary mechanisms of acquired resistance include the following.[26]

Altering enzymes or rendering antimicrobial agents inactive

Both gram-positive and gram-negative bacteria are capable of modifying enzymes or render antibiotics ineffective. In enzymatic modification, acetyl, adenyl, or phosphate groups are added to specific sites on an antibiotic by bacterial enzymes. This chemical alteration inactivates the antimicrobial agent, preventing it from binding to its target site.[27] For instance, phosphorylation happens in macrolides, whereas aminoglycosides either undergo acetylation, adenylation, or phosphorylation. In enzymatic inactivation, antibiotics are primarily degraded through the hydrolytic cleavage action of bacterial enzymes. (such as lactamases against penicillin and cephalosporins) decreased intracellular antimicrobial agent accumulation. To reduce the buildup of antibacterials within bacterial cells, bacteria either use reduced influx or enhanced efflux. Antibiotics, such as tetracyclines and lactam, which enter E. coli by the OmpF and carbapenems, which enter *Pseudomonas aeruginosa* by the OmpD, are thought to enter bacteria through porins, an outer membrane protein (OMP). Porin genes may be downregulated, structurally altered, or even functionally deleted 26. The resistance-nodulation-cell division (RND) family of transporters, such as the AcrAB-TolC system in *E.coli*, is a type of increased efflux mechanism found primarily in Gram-negative bacteria. These transporters actively expel antibiotics from the cells and are commonly used by many bacterial species to remove toxic substances produced during cellular metabolism.[26-28]

Alterations at the antimicrobial agents target sites

Among the changes at the target sites are: Fluoroquinolone resistance is primarily caused by mutations in the quinolone-resistance-determining region (QRDR) in the DNA gyrase (topoisomerase II and topoisomerase IV). This can happen in both gram-positive and gram-negative bacteria. For example, Erm methylases, which target macrolides, lincosamides, and streptogramin B antibiotics, are known to be highly effective in developing resistance in both Gram-positive and Gram-negative bacteria. Additionally, the methylation of the cfr gene has been used to detect resistance in a variety of bacteria, including *Proteus vulgaris, Staphylococcus spp., Enterococcus spp., Bacillus spp., and E. coli*.[29] Resistance to sulphonamide and trimethoprim is frequently caused by the replacement of an origin target that is susceptible to a particular antibiotic with a drug-resistant target. Sul1, Sul2, and Sul3 are genes for dihydropteroate synthases in gram-negative bacteria, which are resistant to sulphonamides.[34,45] Additionally, the mecA and mecC genes in Staphylococcus spp. produce an alternative penicillin-binding protein with a significantly reduced affinity for all β-lactam antibiotics. This alteration disrupts the elongation process and prevents protein synthesis 30. The process of dissemination of resistance gene by Transformation, Transduction, Conjugation, resulting in formation of MDR and XDR multiple drug and extensive drug resistance bacterial strain respectively. The former is resistive to at least one or two drug of any class whereas later is susceptible to one or few class of drug only.

Antimicrobial Activity of Eugenol

The free OH group in the structure of eugenol has been linked to its possible antibacterial effects against a variety of species, including *Staphylococcus aureus, Pseudomonas aeruginosa,* and *Escherichia coli*. Eugenol is a hydrophobic molecule that can easily pierce the lipopolysaccharide cell membrane and enter the cytoplasm. It is thought that this property of eugenol causes it to work against Gram-negative bacteria by disrupting the cytoplasmic membrane. Once within the cell, it has the potential to modify the cell's structure and cause intracellular components to seep out. It has been proposed that the hydroxyl group in eugenol inhibits protease, histidine decarboxylase, and amylase activity in Enterobacter aerogenes by binding to these enzymes.[31] Similarly, eugenol has been found to potentially inhibit the activity of membrane bound ATPase in Listeria monocytogenes and Escherichia coli. Furthermore, it has been observed that traditional antimicrobials exhibit enhanced effectiveness when used in combination.[32] Additionally, eugenol is believed to generate intracellular reactive oxygen species (ROS), which can damage cells by inhibiting cell growth, rupturing cell membranes, and causing DNA destruction.[33] *Streptococcus agalactiae* (planktonic GBS—group B streptococci strain) human isolates, including those resistant to erythromycin and clindamycin, were observed to develop less rapidly when exposed to eugenol.[34] The GBS planktonic cells exhibited leakage of proteins and lipids from the cytoplasm and rupture of the cell membrane after a five-hour incubation with 0.125% to 0.5% eugenol.[35] The minimum inhibitory concentration (MIC) for the derivatives

was found to be 500 µg/mL, compared to 1000 µg/mL for eugenol. Additionally, eugenol derivatives demonstrated stronger antibacterial activity than eugenol itself. The derivatives were synthesized by adding functional groups to the double bond of the allyl group or by esterifying the hydroxyl group (-OH) with various carboxylic acid derivatives.

Eugenol has demonstrated antiviral activity alongside its potent antibacterial properties. It works synergistically with acyclovir to inhibit the herpes virus in vitro, including HSV-1 and HSV-2 (Herpes simplex virus types 1 and 2), by limiting viral infection and preventing replication. Eugenol has also been found to possess antifungal activity against a range of fungal strains in vitro, including *Candida albicans, Aspergillus niger, Penicillum glabrum, Penicillum italicum, Fusaria oxysporum, Saccharomyces cerevisiae, Trichophyton mentagrophytes, Lenzites betulina, Laetiporus sulphurous, and Trichophyton rubrum*. Eugenol is hypothesized to interfere with the function of cell membranes in fungi, suppress virulence factors, and impede the development of fungal biofilms.[36] Sharifzadeh and Shokri used the broth microdilution test and the checkerboard microdilution method to assess the antifungal activity of eugenol and its potential synergistic effects with voriconazole against Candida strains isolated from mares' reproductive systems. The minimum inhibitory concentrations (MICs) of eugenol were 400–800 µg/mL for Candida tropicalis and 200–400 µg/mL for Candida krusei. When combined with voriconazole, eugenol showed synergistic effects against *Candida tropicalis (83.3%)* and *Candida krusei (77.7%)*, with no evidence of antagonistic activity. As a result, eugenol has the capability to be an effective antifungal medication for treating genital Candida yeast. Additionally, the combination of eugenol and voriconazole could be effective in reducing antimicrobial resistance in mares with genital candidiasis.[32] According to a study on eugenol, when paired with different antibiotics like vancomycin, penicillin, ampicillin, and erythromycin, the MIC values could be reduced by as much as 5-1000 times more compared to when the individual antibiotics were used alone. Furthermore, it has been shown that eugenol enhances the bacterial cell membrane-damaging effects of lysozyme and SDS. Limiting the usage of antibiotics to natural substances like eugenol appears to be a feasible answer because the widespread use of antibiotics contributes to the emergence of antibiotic-resistant bacterial strains.[37] Eugenol's capacity, as an ingredient in essential oils, to remove bacterial biofilm has been investigated, along with that of other substances such trans-cinnamaldehyde, citronellol, and terpineol. A three-dimensional microcolony of bacteria that is embedded by an extracellular matrix is known as a bacterial biofilm.[38] A serious issue is bacterial biofilms. For instance, they can proliferate on the surface of food products in the food industry, contaminating the food and potentially causing disease. Effective solutions are therefore being sought to resolve this issue.[39] The aforementioned substances, which are elements of essential oils, were tested by Olszewska *et al*.[39] for their capacity to prevent the development of the *Escherichia coli* biofilm. The study utilized platelet count, resazurin test results, and Syto® 9/PI (propidium iodide) staining, along with flow cytometry (FCM) and confocal laser scanning microscopy (CLSM). With a concentration of 3 mM, eugenol significantly reduced the metabolic behavior of bacterial cells that are a part of the biofilm (49%), as well as their capturability (84%). However, eugenol demonstrated the least capacity to harm the microbial cell membrane when compared to the other compounds tested. Another frequent source of bacterial infection is the biofilm that bacteria create on biomaterials and medical implants. A hydrophilic copolymer system based on eugenol was discovered to successfully stop the growth of these bacteria in studies. Eugenol affects bacterial biofilms in general by inhibiting biofilm development and decreasing the vitality of cells that produce biofilms. The inactivation of bacterial biofilm cells, cell dispersion within the biofilm matrix, and reduction of biofilm-associated gene expression, such as that of the pgaA gene, were additional impacts. Eugenol may also limit the development of biofilms and impede the synthesis of bacterial virulence factors such violacein, elastase, and pyocyanin. Additionally, *Salmonella enteritidis* and other multi-resistant bacteria seem to be susceptible to its effects.[40] Antimicrobial activity against carbapenem-resistant *Klebsiella pneumoniae* (CRKP) was also demonstrated by Qian *et al*. As a result of its resistance to antibiotics and antimicrobials, *Klebsiella pneumoniae* is a highly pathogenic bacterium that poses a serious threat to both humans and animals. This bacterium demonstrates a variety of virulence traits, including as the capacity to form biofilms and the presence of outer membrane proteins and capsular polysaccharide. Finding a powerful drug to fight or weaken this virus is crucial since carbapenem-resistant CRKP strains pose a particularly serious threat. Given that it has shown multidirectional activity, eugenol appears to be a promising

chemical with antibacterial activity against this pathogen. By using the agar dilution method, the minimal inhibitory concentration (MIC) of eugenol was found to be 0.2 mg/mL against the four tested CRKP isolates. The extent of cell damage and the number of damaged cells both increased with higher concentrations of eugenol, which is significant. Eugenol's antibacterial effect was caused by damage to the cell membrane, this damage included membrane rupture and cell enlargement, hyperpolarization of the membrane and increased membrane permeability, and, eventually, leaking of intracellular components from CRKP cells. Eugenol has been employed in dental and oral care since ancient times. It has disinfectant properties, antimicrobial activity against bacteria linked to dental caries and periodontal disease, and has been found to relieve local pain from conditions like pulpitis and dentinal hypersensitivity as a topical analgesic. It is mixed with zinc oxide in dentistry to create an amorphous chelate substance that is used to cover the pulp inadvertently, dress endodontic therapy, and temporarily fill cavities. Furthermore, it can be used in liquid form to fill root canals with specialty pastes such mummification pastes (such as Caryosan and Endomethazone). Additionally, eugenol is sometimes applied to the gums to numb them prior to the insertion of dentures. Eugenol is frequently used in pharmaceuticals, food, cosmetics, and as a local antiseptic and analgesic due to its multidirectional action and reputation as a usually safe chemical at low concentrations. In addition, it is frequently found in home products including soap, perfume, skin care items, and cigarettes where it serves as a flavor and scent. In addition to being a pesticide and fumigant, it is also employed as a preservative to safeguard foods against microbes. The maximum daily intake of eugenol or clove oil for humans is 2.5 mg/kg body weight, according to the Joint Food and Agriculture Organization/WHO Expert Committee on Food Additives.[41] Due to its beneficial effects on health, eugenol is also used to treat joint pain and infections of the upper respiratory and gastrointestinal tracts. Additionally, eugenol is a component of several medications used to treat upper respiratory tract mucosal inflammation and for cold prophylaxis. Amol, Aromatol, or Olbas are a few examples of drugs that are frequently given as inhalation and aerosol therapy.[42] Eugenol has uses in food production and agriculture due of its multifaceted antibacterial and antifungal properties. An essential benefit is that its favorable effect is linked to low concentrations of active ingredient. Additionally, eugenol is effective against a range of foodborne pathogens (such as *Aspergillus ochraceus* and *Salmonella typhi*), therefore using it helps avoid acute food poisoning. Eugenol has shown to have anti-salmonella activity by reducing the permeability of the pathogen's cell membrane, which is followed by ion leakage, loss of cellular content, and eventually cell death.[32-41] Eugenol is therefore utilized as a biocontrol agent for grains in agriculture because it has been discovered that it may lessen Salmonella contamination of organic goods by inhibiting its proliferation in soil. Eugenol has the ability to prevent Aspergillus ochraceous from producing ochratoxin A. Fruits including strawberries, apples, and peaches as well as their juices are shielded from microbes' damaging effects by its antifungal characteristics *Staphylococcus aureus* is one of the primary prevalent infections associated with food. According to studies, eugenol inhibits the synthesis of toxic shock syndrome toxin 1, staphylococcal enterotoxin A and B, and alpha-hemolysin as well as the expression of these toxins in S.*aureus*.

However, eugenol can be pro-oxidative and potentially hazardous at high concentrations; the FAO deems levels below 2.5 mg/kg body weight as safe. Additionally, eugenol may occasionally cause allergic reactions, such as allergic contact dermatitis, particularly among dental professionals. Eugenol derivatives represent a significant area of research and hold promise as components in insecticides and pesticides.[41]

CONCLUSION

Eugenol is valued for its broad spectrum of biological activities and has various applications. It is commonly used as a fragrance in soaps and perfumes, but it also plays a role in pharmacology and medicine. Its primary uses include serving as a local analgesic, antiseptic, and anti-inflammatory agent in inhalation and aerosol therapies. Notably, eugenol has demonstrated therapeutic potential in medications for cancer treatment. Furthermore, it enhances the efficacy of several antibiotics, including vancomycin, penicillin, and erythromycin, by increasing their potency and lowering their minimum inhibitory concentration (MIC), which helps reduce pathogen resistance to antibiotics. Despite its benefits, careful dosing is required due to potential toxicity at high concentrations, and it may cause allergic reactions in sensitive individuals.

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Review Article

Journal of Biochemistry and Biophysics
Volume 9 Number 1, June - December 2024
DOI: http://dx.doi.org/10.21088/rfpjbb.2582-3558.9124.4

Oocyte Quality & its Impact on the Reproductive Outcomes of Women Undergoing Assisted Reproduction: A Review

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How to cite this article:

Richa Saxena, Nidhi Srivastava, Oocyte Quality & its Impact on the Reproductive Outcomes of Women Undergoing Assisted Reproduction: A Review. RFP Jour. of Bio. and Biophy. 2024;9(1): 091–096.

Abstract

The Assisted Reproductive Technology (ART) has led to technical advancements in the last few years. These techniques have greatly assisted in achieving an acceptable pregnancy rate. Pregnancy followed by delivery signifies the success of an ART treatment. The success rate of an ART treatment is hinged on various parameters of which oocytes have a primary role in fertilization, early embryo development and its subsequent implantation. Successful pregnancies are common in assisted reproductive technology clinics because of invasive and non-invasive methods used to isolate biologically competent oocytes. The process of fertilizing the embryo, early embryo growth, implanting of the fertilized embryo, and favorable pregnancy results may be predicted by morphological features like zonapellucida, the cumulus complex, first polarized body, perivitelline membrane area space, spindle formation assembly, and ooplasm. The non-invasive assessment of oocyte quality based on cumulus gene expression analysis in conjunction with morphology assessment can improve the clinical pregnancy (CPR) and live birth rates (LBR). The infertility that is linked with poor oocyte quality may be explained by a number of different processes that are not exclusive to one another. To a large extent, the success of in vitro fertilization (IVF) depends on the oocyte, which plays a critical role in defining embryonic competence. It has been suggested in research studies that the shape of oocytes may serve as a non-invasive indicator of the quality of the oocytes. The current review investigates the correlation of oocyte quality and its effect on the clinical outcomes of women undergoing regulated ovarian stimulating for an intracytoplasmic sperm injection (ICSI).

Keywords: Embryo, Pregnancy, In-vitro fertilization, Endometriosis, Polycystic ovarian syndrome.

INTRODUCTION

Extending endometrial or stroma tissues beyond the uterine cavity is a diagnostic criterion for endometriosis.[1] Women of reproductive age (10–15%) and those receiving infertility treatments (25%–50%) might be affected. The American Fertility Society's grading system for the severity of the condition, which is based on the outcomes of laparoscopic procedures, is extensively utilized

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Received: 14.06.2024 **Accepted:** 17.08.2024

by practitioners. However, when it comes to characterizing severe endometriosis, this anatomical categorization falls short. There is just a weak relationship between this and the level of the patient's symptoms, and it is not a good predictor for whether a pregnancy would occur naturally or be induced. Endometriosis may manifest itself clinically in a wide variety of ways, and these variations have been attributed to a wide range of pathophysiological mechanisms.[1] Most clinicians like to entertain many hypotheses. Genetics, hormones, immunology, angiogenesis, and the environment have all been demonstrated to have a role in the development of endometriosis.[12] Oocyte size has been proposed as a non-invasive indicator of oocyte quality in certain published works.[1] Some morphological flaws, detectable with a light microscope, were linked to poor oocyte quality by Tus, Van Blerkom, and Henry.[7] Cumulus cells, nucleus development, and cytoplasmic and extra-cytoplasmic features are examined to establish oocyte morphology.[1] Polycystic ovary syndrome (PCOS) is diagnosed in almost a quarter of infertile couples, and its incidence in asymptomatic people is estimated at 33%.[12,13] The endocrine, metabolic, and reproductive systems are all affected by polycystic ovary syndrome[14], making it a complicated multi-spectrum illness. The hyperandrogenic condition in PCOS is the root cause of decreased folliculogenesis.[15] The most frequent non-invasive evaluation techniques are now focused on the morphology and developmental parameters of embryos during in vitro development.[16] Only around 5% of new oocytes result in a live-born kid, according to a clinical investigation that evaluated the true biological effectiveness of IVF by measuring the percentage of live births in proportion to the number of oocytes extracted.[18] Because gonadotrophins increase the number of follicles and accessible oocytes, they have significantly improved the success rate of in vitro fertilization.[19] By stimulating ovarian follicles, retrieving follicular fluid, and isolating and vitrifying mature oocytes, the method is known as oocyte cryopreservation (OC).[20]

Over the past few years, there has been a decline in the number of individuals across the globe that has difficulties with reproduction. PCOS is a potential cause of anovulatory infertility, however, it is treatable. The layer of pellucid zonal, polarized body formation, cumulus-oocyte, and the internal features of oocytes have all been connected to the process of fertilizing the embryo, formation of cleavages and splits in the embryo, and the development of the outcomes of the process of embryo fertilization clinically in the ART Laboratory.[2] Oocyte chromatin aligns in metaphase two (MII) in the equatorial region of the meiotic spindles (MS).[2] Infertile women with polycystic ovary syndrome (PCOS) have two assisted sexual treatment options: controlled ovarian hyperstimulation (COH) and in vitro maturity (IVM) therapy. The increasing global incidence of infertility may be attributed to several causes, including older mothers and the stresses of contemporary life. For this reason, ART's significance grows constantly. Although ART has improved in efficiency and accuracy, the success rate is still only about 35% when measured by the number of live births per transplanted embryo.[4] PCOS is a hormonal disorder that mostly affects reproductive-aged women. The Rotterdam criteria for PCOS involve the presence of medical and/or quantitative hyperandrogenism, ovarian dysfunction, and polycystic ovary shape (PCOM). Nearly a quarter of couples who are infertile are diagnosed with the polycystic ovarian syndrome (PCOS), and its occurrence in asymptomatic persons is put at 33%.[5] Embryos that were developed in vitro have not shown the same potential for attachment as embryos that matured in vivo. This is because a healthy kid is more likely to grow from an egg that has been allowed to mature in vivo. The poor growth of embryos observed in in vitro developed human oocytes has been linked to a failure to synchronize the process of maturation in the cytoplasm and the nucleus of the developing and growing embryo. While the relationship between metaphase II (MII) ovarian shape and the success of the process of fertilization taking place in vitro is well established in conventional IVF, it is less clear after sperm injection taking place intracytoplasmic-ally (ICSI). Only two of the studies found any connection between morphologic abnormalities and the fertilization and quality of the embryos produced by ICSI. Despite good fertilization, embryo quality, and live birth rates, oocytes with cytoplasmic abnormalities have been shown to have a lower implant rate and a lower rate of sustained pregnancy.[6] It has been discovered that the shape of the first polar body and other extracytoplasmic abnormalities observed at the time of ICSI are accurate indicators of subsequent development and embryo quality. Furthermore, it has been found that the elective transplanting of eggs selected based on these features has been linked to higher implanting and pregnancy rates. These studies show that aberrant MII oocytes have a reduced likelihood of the process of fertilization cleavage and embryonic viability compared to

normal oocytes. The morphology of MII oocytes generated in vitro has not been studied before.[6] In vitro fertilization (IVF) has been around since 1978, when the first kid conceived with the help was born. Since that time, ART has expanded considerably, resulting in the birth of over 8 million children with the use of IVF across the world.[21]

Significant progress has been made in the field of human-assisted reproductive technology in recent decades, from in vitro ovarian maturation and fertilization through animal cloning. In general, the scientific literature agrees that oocyte quality is the most important factor in determining successful fertilization, initial growth, and implantation. Therefore, the success of infertility treatment operations may depend on several factors, the most important of which is the quality of the oocytes used in the processes. This study set out to do just that, reviewing the tools and standards used to evaluate oocyte quality morphologically.[23] Recent decades have seen extensive research into assisted reproductive technology for humans, leading to substantial progress in this field. This includes anything from the maturation and implantation of oocytes in vitro to the cloning of animals. The quality of the oocytes is the single most important factor in determining the success of fertilization, early growth, and implantation, according to the research. Consequently, the success of treatment for infertility treatments may depend on several factors, the most important of which is the quality of the oocytes used in the operations. The purpose of this study was to provide a comprehensive overview of the techniques and standards currently in use for morphologically evaluating oocyte quality.[24]

Numerous studies have examined the correlation between oocyte excellence, embryo growth, and successful in vitro fertilization, also known as IVF.[23] When choosing embryos for transfer, morphology is used almost entirely by most IVF clinics, including ours. Our weekly examination of unsuccessful IVF cycles has shown that oocyte evaluations are often more predictive of IVF success than embryo evaluations. We postulated that oocyte-level prediction of pregnancy success, rather than embryo-level prediction, could provide more useful information when choosing embryos for transfer. Future perspective research was created to examine this hypothesis. The quality of the embryo is now the strongest predictor of a successful pregnancy; hence researchers have focused nearly entirely on enhancing embryo evaluations rather than oocyte evaluations. This has recently led to a rise in the use of high-priced closed robotic incubation systems that rely on time-lapse imaging.[23] Taking into account the exorbitant price of IVF, it makes sense financially to choose embryos more efficiently. Consequently, we prospectively studied a new, simple oocyte scoring method and contrasted it to the older, more widely used day 3 embryo evaluations currently used by the majority of IVF clinics.[23]

Assessment of the quality of the oocyte required further for the AZT technique:

Oocyte and embryo classification was the subject of a 2011 meeting of experts. These previously established guidelines are now being updated to account for new information and technological capabilities. The progression of the oocyte's nuclei & and cytoplasm is directly linked to the formation of a human embryo. Oocyte quality has been hypothesized to be reflected in cytoplasmic characteristics such as cytoplasmic homogeneity, the presence of vacuoles, and the formation of smooth clumps of the endoplasmic reticulum.[8] There have also been suggestions about extracytoplasmic characteristics, such as the initial polarized body form, perivitelline temporal dimensions, zonapellucida failures, and shape.

Factors affecting oocyte quality:

Factors including smoking, alcohol usage, obesity, a woman's age, endometriosis, assisted reproductive technology (ART), and genetic abnormalities like hormone receptor polymorphisms may all have a detrimental impact on oocyte quality. Biochemical and morphological alterations in oocytes have been linked to a rise in ROS, or reactive oxygen species, a type of oxygen, which may occur as a result of systemic diseases. Oocyte dysmorphism may manifest internally or externally in the cell. Preimplantation testing development failure is proportional to the degree and number of oocyte morphological abnormalities. The lady had four rounds of IVF, all of which resulted in dysmorphic oocytes. Aiming to connect the dots between the oocyte characteristics stated in the case reports aboutthe authenticity of the oocyte and the size reported in the study cited in the review, this literature review seeks to conclude the nature of these connections.[9]

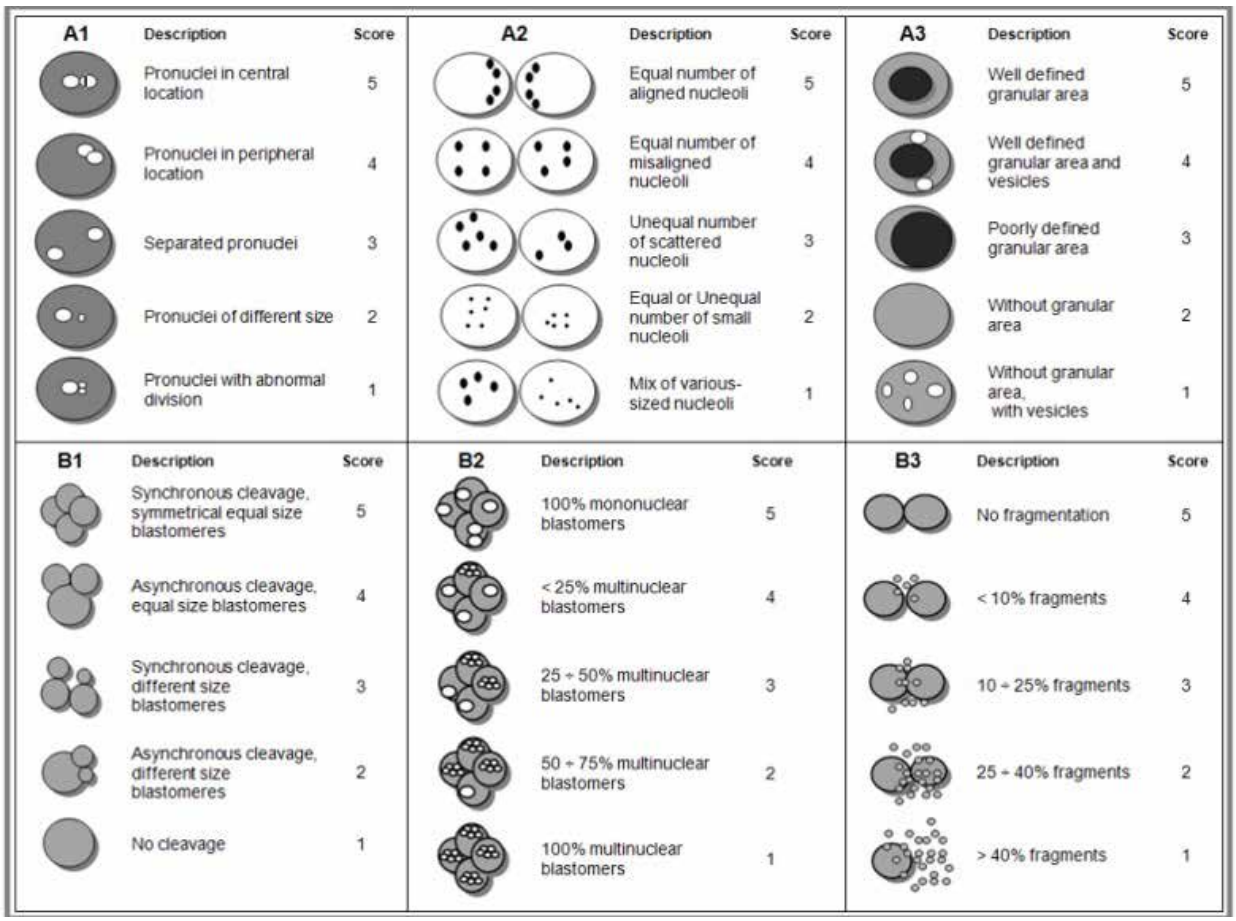

Fig. 1: shows the different oocyte assessment methods[22]

Grade	Rating	Description
		<10%fragmentation
1	Good	Stage-specific cell size
		No multinucleation
		10 – 25% fragmentation
2	Fair	Stage-specific cell size for majority of cells
		No evidenceof multinucleation
		Severe fragmentation (.25%)
3.	Poor	Cell size not stage specific
		Evidence of multinudeation

Fig. 2: Shows the grading system for oocytes[25]

Pregnancy outcomes related to the use of the technique of assisted reproductive technique:

The proportion of live births that may be attributed to fresh embryo transfers, which includes cycles of IVF and ICSI, climbed from 33.3% in 2007 to 36.5% in 2009. This is a significant increase. The abortion rate per implantation averaged 5.3% between 2007 and 2009. Only 2.5% of all live births that followed fresh embryo transfer (including those that followed IVF and ICSI) were ectopic. This value didn't alter at all during the course of the study's three years. The incidence of ectopic pregnancies is much lower than the globally estimated rate of 2% per recorded pregnancy. The rates of multiple births were also calculated. About 74% of births were to a single mother during the research period, whereas 22% were to a set of parents. Statistics on the prevalence of preterm and full-term births, as well as perinatal illness and death, were not provided. The number of cycles when frozen embryos were transferred after being artificially treated with hormones rose between 2007 and 2009. Matching years' numerical sums grew from 1525's to today's 2678's. The percentage of women who waited for their menstrual cycle to begin before preparing for an embryo freeze transfer (FET) fell from 45% in 2007 to 27% in 2009. Using exogenous hormones to stimulate the endometrium's natural maturation process eases physicians' concerns about using synthetic cycles. The total amount of FET cycles increased from 1954 to 3087 between 2007 and 2009. From 2007 to 2008, the proportion of FET cycles in which just one embryo was transplanted fell from 9.46% to 7.87%.

The number of women using donor eggs, whereby oocytes are obtained from strangers, doubled from 2007 and 2009. From 1047, we are now 2130 strong. There was only a 20% rise in the number of eggs donated by known or related donors. The rise in media attention given to organizations that popularized the field of reproductive technologies for assisted living may explain why customers prefer anonymous donors: more women may come forward to offer their services as skilled donors in exchange for financial payment. It is not known how frequently one donor may provide oocytes to many recipients.[11]

Women around the age limit of 45 made up the bulk of egg donors' recipients. There was a consistent pattern over all three years. In the study, women aged 55 and above made up around 1.18 percent of the egg recipients. Better techniques for tracking patients for health risks like diabetes, hypertension, as well as coronary heart disease have contributed to the recognition that conception in the postmenopausal group of women may be unphysiological, potentially endangering the health of the mother. That's why a lot of docs advise against becoming pregnant beyond 50.[11]

CONCLUSION

When assessing physical characteristics, some ART clinics utilize light or polarized microscopes. As a consequence, this has the potential to aid in the choosing of high-quality oocytes, a step crucial to enhancing the rate at which healthy infants are born. Meiotic spindle, the amount of cyclin-dependent kinase (CDK) activity, cyclin-dependent phosphatase (CPP) activity, vacuoles/refractive organizations, oocyte shape, granulation, which and ooplasm viscosity are among oocyte morphologies that are routinely examined. For oocyte selection, it is unclear which of these variants is optimal. Using a mix of morphological evaluations, it may be feasible to reliably predict which oocytes will end up incapable of early embryos. Oocytes with obvious or slightly fragmented cytoplasm, a small PS, a presumably intact PB, typically apparent meiotic spindle-like as well as CC, and colorless as well as birefringentZonapellucida ought to be chosen for the initial administration of ARTs in the absence of additional constraints like the age of the patient, collected oocyte numerals, or previous ART failures. Particularly important is the evaluation of these morphological parameters in an extensive group of similar patients across a wide variety of ART centers.[10]

Predictions of oocyte quality might be improved by combining morphological studies with modern technologies like as genome sequencing, transcriptomics, proteomics, and metabolomics. Selecting embryos with desirable physical characteristics and, in certain situations, genetic testing before implantation for aneuploidy testing might increase the success rate of fertility treatments such as fertilization taking place in-vitro and injection of sperm (IVF/ICSI) taking place in an intracytoplasmic way and procedures to reduce the occurrence of multiple embryos during pregnancy. Early embryos are being tested for desirable morphological, metabolism, proteomic, epigenetic, and genome characteristics. In circumstances where a relatively small amount of oocytes may be retrieved owing to poor fertility or regulatory limits, morphological features for choosing competent oocytes may still be employed despite their lower therapeutic effectiveness than first envisaged.[10]

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