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Nature's Answer to PCOS: Exploring the Therapeutic Potential of Caesalpinia bonducella

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Abstract: ***Caesalpinia bonducella (L.) Fleming, also known as Caesalpinia bonduc (L.) Roxb. and Caesalpinia crista Linn., belongs to the family Caesalpiniaceae. It is a spiny shrub found worldwide, particularly in India, Sri Lanka, and the Andaman and Nicobar Islands, thriving mainly in tropical regions. This plant is highly valued in traditional medicine due to its therapeutic properties, with all parts being utilized for medicinal purposes.***

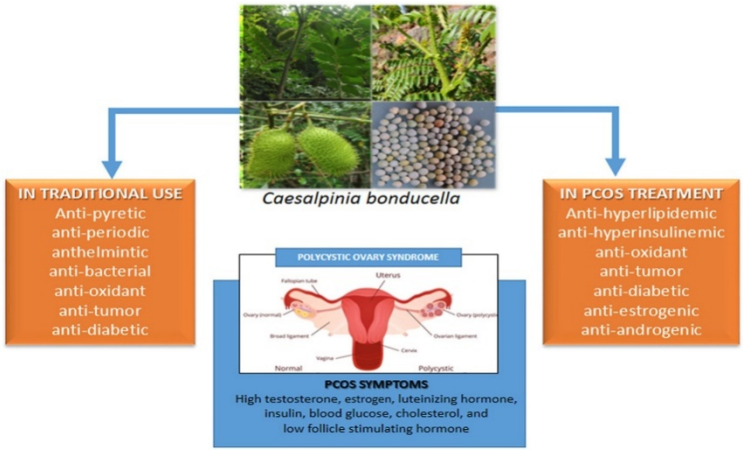
It has been reported to exhibit a wide range of pharmacological activities, including anxiolytic, antinociceptive, antidiarrheal, antidiabetic, adaptogenic, anthelmintic, antiestrogenic, anti-inflammatory, antimalarial, antimicrobial, antifungal, antispasmodic, antioxidant, antiproliferative, antipsoriatic, antitumor, larvicidal, muscle contractile, hepatoprotective, anticonvulsant, and antifilarial effects.

Phytochemical analysis of its seeds has identified the presence of various bioactive compounds such as alkaloids, flavonoids, glycosides, saponins, tannins, and triterpenoids.

This species is widely recognized for its medicinal and therapeutic significance in Indian AYUSH systems, including Ayurveda, Unani, and Siddha. COVID-19, a contagious disease cause by the novel Coronavirus (SARS-CoV-2), is primarily characterized by symptoms such as fever, fatigue, and dry cough.

To strengthen immunity and alleviate symptoms of upper respiratory tract infections, the Ministry of AYUSH, Government of India, has provided guidelines for qualified Unani practitioners, emphasizing a prophylactic approach. Among the recommended single drugs is Karanjwa, known for its antipyretic, antimicrobial, anti-inflammatory, and immunomodulatory properties.

Graphical Abstract



I. INTRODUCTION

Medicinal plants have gained significant importance in global healthcare for both humans and animals, serving not only as remedies for diseases but also as resources for maintaining overall well-being. However, understanding the specific constituents responsible for their therapeutic effects is essential. This necessitates the extraction, isolation, and identification of bioactive compounds. The extraction of plant-based drugs is primarily done using solvents, with conventional methods including maceration, percolation, decoction, digestion, and hot continuous extraction.

In recent years, there has been a growing interest in plant-based research, leading to a substantial body of evidence supporting the medicinal potential of various traditional herbs. Many widely used pharmaceutical drugs have origins in plant extracts, and herbs are extensively used to manage conditions such as cardiovascular diseases, liver disorders, central nervous system issues, and metabolic disorders. Due to their ability to provide significant therapeutic benefits, medicinal plants and their extracts are considered valuable for drug development and supplementation. Numerous herbal compounds have demonstrated a broad range of biological activities and continue to be used in traditional medicine and as dietary supplements for various ailments.

Caesalpinia bonducella (L.) Fleming, also known as Caesalpinia bonduc (L.) Roxb. and Caesalpinia crista Linn., belongs to the Fabaceae/Caesalpiniaceae family. It is a thorny shrub widely distributed across tropical regions, particularly in India, Sri Lanka, and the Andaman and Nicobar Islands. Recognized for its medicinal value, all parts of the plant are utilized in traditional medicine. The plant has been reported to exhibit pharmacological activities such as anxiolytic, antinociceptive, antidiarrheal, and antifilarial effects.

Phytochemical studies on Caesalpinia bonducella seeds have identified the presence of several bioactive compounds, including alkaloids, flavonoids, glycosides, saponins, tannins, and triterpenoids. The species name “Bonducella” originates from the Arabic word “Bonduce,” meaning “little ball,” referring to the globular shape of its seeds. The seeds, which are gray in color and resemble eyeballs, are called Kuberakshi in Sanskrit, meaning “eyes of Kubera,” the Hindu god of wealth.

The plant has often been confused with Caesalpinia bonducella (syn. C. bonduc) and has been described under the same name. Additionally, species such as C. nuga and C. jayoba are sometimes incorrectly classified as synonyms for C. crista, although C. jayoba is actually an adulterant of C. crista.

II. CAESALPINIA BONDUCELLA AND PCOS TREATMENT

Polycystic Ovary Syndrome (PCOS) is a common endocrine disorder affecting young women, characterized by hyperandrogenemia, hyperinsulinemia, and dysfunction in the ovarian and hypothalamic-pituitary axis. Women with irregular menstrual cycles and polycystic ovaries may be diagnosed with PCOS, even in the absence of clinical or biochemical signs of androgen excess. The condition presents with diverse symptoms, influenced by factors such as prenatal androgen exposure, genetic predisposition, nutritional status during fetal development, insulin resistance, exaggerated adrenarche during puberty, and body weight fluctuations. Caesalpinia bonducella has been found to be effective in managing PCOS.

The species name "bonduc" originates from the Arabic word Bonduce, meaning "little ball," referring to the globular shape of its seeds.

The seeds are gray in color and resemble eyeballs, which explains their Sanskrit name Kuberakshi, meaning "eyes of Kubera," the Hindu god of wealth.Traditionally, a decoction made from roasted seed kernels has been used to treat asthma. A paste made from the kernels is known to provide relief from boils and similar swellings. The seeds of Karanjwa are believed to have styptic, purgative, and anthelmintic properties, and they are used in the treatment of inflammations, colic, malaria, hydrocele, skin diseases, and leprosy.

Pharmacological studies on Karanjwa seeds have revealed a wide range of therapeutic properties, including antidiarrheal, antiviral, antibacterial, antimicrobial, antifungal, antidiabetic, antitumor, antipyretic, analgesic, antifilarial, anxiolytic, anti-inflammatory, antioxidant, immunomodulatory, and trypsin and chymotrypsin inhibitor effects.

Among the various AYUSH systems, Ayurveda and Unani have long histories of utilizing medicinal plants for therapeutic purposes. The Unani System of Medicine (USM), which originated in Greece, later spread to India, where it became an established traditional medical system.

Karanjwa is widely used in Ayurveda, Unani, and Siddha (ASU) systems, with its therapeutic applications varying based on preparation and usage. In Ayurveda, it is employed for the treatment of conditions such as tumors, cysts, and cystic fibrosis.

III. DESCRIPTION

Caesalpinia bonduc (L.) Roxb.

A. Current Scientific Name

-Caesalpinia bonduc

B. Authority

-(L.) Roxb.

C. Synonyms

1) Caesalpinia bonducella (L.) Fleming
2) Caesalpinia crista Thunb.
3) Guilandinabonducella L.
4) Guilandinabonduc L.
5) Fever nut

D. Classical Names

1) Ayurveda: Kantakikaranjah, Kuberakshi, Latakaranja, Puti, Morata, Putikaranja
2) Unani: Karanjawa
3) Siddha: Kazharchikkaai

E. Vernacular Names

1) English: Bonduc Nut, Nicker Bean
2) Hindi: Gachika, Gajga, Kanderi, Kantikaranja, Naktamala, Karanj
3) Kannada: Gajaga, Heggajjiga, Kitta, SannaGajjuga
4) Malayalam: Caretti, Kalanchik-Karu, Kalanci, Kulunje, Avil, Kalimarakam
5) Marathi: Gajaga, Kanchaki, Karbath, Rahedo, Saagaragota
6) Tamil: Cakarakoti, Carivacantam, Gech-Chakkay, Kaccakkay, Utarikkoti
7) Telugu: Gachakaya, Thellagachha, Gutsakai, SukaJambuka, Yalakhi
8) Arabic: Akitmakit, Hajra Ilaqi, Hajra-ul-Aqaab, Hajra-ul-Masak, Hajra-ul-Nasara
9) Persian: Ashak-e-Marium, Khayahe-i-Iblis, Khayahe-Iblis, Qana-e-Iblees

F. Classification (Bentham and Hooker System)

1) Kingdom: Plantae (Plants)
2) Division: Tracheophyta (Vascular plants)
3) Class: Magnoliopsida (Dicotyledons)

4) Order: Fabales
5) Family: Leguminosae (also known as Fabaceae)
6) Subfamily: Caesalpinioideae
7) Genus: Caesalpinia L.
8) Species: Caesalpinia bonduc (L.) Roxb.

G. Citations

Caesalpinia bonduc (L.) Roxb. Fl. Ind. 2: 362. 1832.
Emended by Dandy & Exell in J. Bot. 76: 175. 1938.
Saldanha & Nicolson, Fl. Hassan 871. 1978.
Guilandina bonducella (L.) Flem. Asiat. Res 11: 159. 1810. (nom. illeg.).
FBI 2: 254. 1878.
Caesalpinia crista auct, Gamble 1: 393. 1919.

H. Habitat

Commonly found in hedges, scrub forests, open areas, plains, and sacred groves.

I. Habit

A large, sprawling, and thorny perennial shrub.

J. Stem

- Grayish in appearance, covered with downy hairs.
- Armed with sharp, curved, and straight yellow prickles.

K. Leaves

1) Bipinnate, measuring 15–22 cm in length.
2) Composed of 4–6 pairs of pinnae, with prickles.
3) Leaflets arranged in 7–9 pairs, ovate to elliptical in shape, measuring 1.5–3.5 cm in length and 1–2 cm in width.
4) Upper surface smooth, lower surface covered in fine hairs.
5) Base truncate or rounded, margins entire, apex obtuse with a small pointed tip.
6) Petiole approximately 1 mm in length.
7) Stipules are leafy in structure.

L. Inflorescence

Bears long-peduncled terminal and axillary racemes.

M. Flowers

Flowers are pale yellow, measuring about 1.2 cm in diameter.Found in terminal and supra-axillary spicate racemes.Calyx tube is bell-shaped, approximately 5 mm long, with a swollen base.Sepals are five in number, unequal, oblong to obovate, measuring 4.5–5 mm by 1 mm, and covered in fine hairs.Petals are five, oblanceolate in shape, with the upper petal being smaller (5 × 2 mm), while lateral petals measure 5–6 × 1.5–2.5 mm, with an obtuse apex and yellow markings.Stamens are ten, declinate, arranged alternately with five long stamens (up to 5 mm) and five short ones (up to 4 mm).Filaments taper at the base and are covered with glandular hairs, measuring up to 3 mm.Ovary is stalked, globular, about 3 mm in size.Style is short (up to 2 mm) and covered in fine hairs.

N. Fruit

Pods are oblong-obovoid, slightly flattened, measuring 5–7 × 2.5–4.5 cm.
Brick-red in color, densely covered with sharp prickles.
Apex tapers into a pointed beak up to 1 cm in length.
Dehiscent upon maturity.

O. Seeds

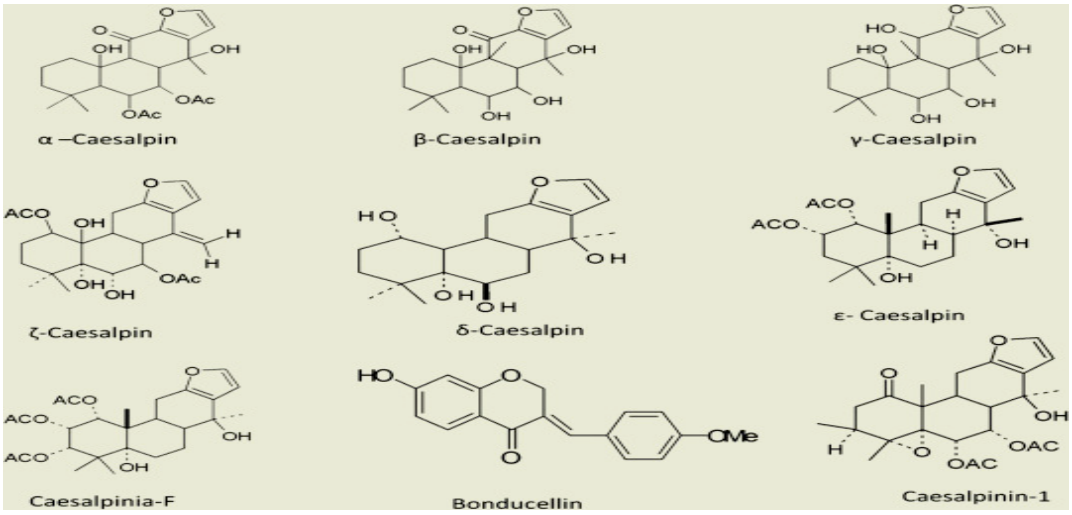
Typically 1 or 2 per pod.
Subglobose in shape, measuring approximately 3 × 6 mm.
Oblong, smooth, and polished with a lead-colored appearance.

Fig. Showing fruits , leaves , flowers and seeds of Caesalpinia bonducella

P. Flowering and Fruiting Season

Flowering: August–October.
Fruiting: December–April.

Q. Chemical Constituents



R. Distribution

The species is widely distributed across tropical regions worldwide (Pantropics).In India, it is commonly found in plains, deltaic regions, and throughout western, eastern, and southern parts of the country.It can grow up to an altitude of 850 m in the Himalayas.Also cultivated as a hedge plant.

IV. TRADITIONAL AND MODERN USES

The seeds of Caesalpinia bonduc are known for their medicinal properties, including styptic, purgative, and anthelmintic effects. They are used to treat inflammation, colic, malaria, hydrocele, skin conditions, and leprosy. In Chennai (Madras), an ointment made from powdered seeds mixed with castor oil is applied externally for hydrocele and orchitis. The seeds are also considered a tonic, febrifuge, and anthelmintic, and are specifically used in the treatment of hydrocele.Seed oil is traditionally used to manage convulsions and paralysis. In Guinea, pounded seeds are believed to have vesicant properties. A mixture of powdered seeds and pepper has been administered to malaria patients, but while it showed mild antiperiodic effects, it was ineffective against severe malaria. The seeds are also ground in water and given to snake-bite victims, though they do not counteract snake venom. A combination of seed and long pepper powders taken with honey is known for its expectorant effects. Additionally, burnt seeds mixed with alum and areca nut serve as an effective dentifrice for treating spongy gums and gum boils. In the West Indies, roasted seeds are traditionally used for diabetes management.

The seed kernel is highly valued for treating simple, continued, and intermittent fevers. A powder made from the kernel, mixed in equal parts with black pepper, is taken three times a day—15-30 grains for adults and 3-4 grains for children. This remedy was officially recognized in the Indian Pharmaceutical Codex, with the prescribed dose being 15-18 grains. It is known to induce perspiration, which helps in fever reduction. A combination of kernel powder, sugar, and goat milk is considered beneficial for liver disorders. Roasted kernel decoction has been used in asthma treatment, while infants who struggle to digest breast milk have been given kernel extract or powder mixed with ginger, salt, and honey for stomach-related benefits. Applying a paste made from the kernel provides relief from boils and swellings.

A medicinal cake, prepared using 30 grains of powdered kernel fried in ghee, taken twice daily, is considered effective in cases of acute orchitis, ovaritis, and scrofula.

1) Roots and Bark

In regions like La Réunion and Madagascar, the root is widely used as a febrifuge and anthelmintic. It is particularly valued for treating leucorrhoea and blennorrhagia due to its astringent properties. In Guinea, a root decoction is prescribed for fever. The root bark is known for its therapeutic applications in treating tumors and facilitating placental expulsion after childbirth. Additionally, it is used to address intestinal worms, amenorrhea, and coughs. In Jamaica, the root is applied topically as a rubefacient and for treating sores.Flowers, Fruits, Leaves, and TwigsFlowers are traditionally used to treat ascites.Fruits are employed in managing urinary disorders, leucorrhoea, piles, and wounds.Leaves and twigs are used in traditional medicine for treating tumors, inflammation, and liver disorders. They are also applied as a remedy for toothaches. Leaf juice has been used in treating conditions like elephantiasis and smallpox.

V. POLYCYSTIC OVARY SYNDROME (PCOS) AND THE ROLE OF CAESALPINIA BONDUCELLA

PCOS is a prevalent endocrine disorder affecting young women, characterized by high androgen levels (hyperandrogenemia), insulin resistance (hyperinsulinemia), and disruptions in ovarian and hypothalamic-pituitary axis function. A woman experiencing irregular menstrual cycles and polycystic ovaries may be diagnosed with PCOS, even in the absence of clinical or biochemical signs of excess androgens. The condition varies significantly among individuals due to factors such as genetic predisposition, prenatal androgen exposure, uterine nutritional status, ethnicity, puberty-related insulin resistance, exaggerated adrenarche, and fluctuations in body weight.

1) Medicinal Potential of Caesalpinia bonducella

Caesalpinia bonducella, also known as Caesalpinia bonduc or Guilandinabonduc, belongs to the Caesalpiniaceae family. It is a thorny shrub commonly found in tropical regions, including India, Sri Lanka, and the Andaman and Nicobar Islands. The plant has a wide range of medicinal uses, including the treatment of PCOS, and is known for its antiseptic, antibacterial, anti-inflammatory, antidiuretic, anthelmintic, antipyretic, anticonvulsant, antidiarrheal, antiviral, antiasthmatic, anti-anaphylactic, antiamoebic, and antiestrogenic properties.

Phytochemical analysis of ethanolic extracts of C. bonducella has revealed the presence of flavonoids, saponins, alkaloids, steroids, and resins, indicating its therapeutic potential. Traditional Ayurvedic and Siddha medicine reports suggest that consuming the seed kernel of C. bonducella has helped many individuals reverse PCOS symptoms.

2) Causes of PCOS

PCOS is primarily driven by hormonal imbalances, particularly elevated insulin levels that stimulate ovarian cells to produce more testosterone while reducing follicle-stimulating hormone (FSH). This results in a higher luteinizing hormone (LH)/FSH ratio, leading to impaired follicular development and ovarian dysfunction. Additionally, changes in the hypothalamus affect the production of gonadotropin-releasing hormone (GnRH), which regulates the pulsatile secretion of LH and FSH from the pituitary gland. Some individuals with PCOS exhibit high estrogen levels and low testosterone, leading to negative feedback inhibition that suppresses FSH release via the GnRH pathway. This hormonal imbalance results in poor follicular maturation.

PCOS has also been linked to oxidative stress and chronic low-grade inflammation. Recent studies have identified hyperandrogenemia (HA) and insulin resistance (IR) as core contributors to the disorder.

3) Genetic and Pathophysiological Aspects of PCOS

PCOS has a strong genetic component, with a 70% concordance rate among monozygotic twins, suggesting a hereditary influence on its pathophysiology. First-degree relatives of individuals with PCOS often exhibit both metabolic and reproductive issues. Research indicates that girls with a genetic predisposition to PCOS can show signs of glucose-stimulated hyperinsulinemia as early as age four, continuing into puberty.

Studies on peripubertal girls with PCOS-affected mothers have revealed pancreatic β-cell dysfunction, contributing to impaired insulin regulation. This dysfunction is potentially linked to the TCF7L2 gene, which is associated with type 2 diabetes. Epigenetic modifications, such as alterations in the PDX1 gene, which regulates pancreatic development, may also play a role. Elevated levels of the adaptor protein Lnk have been found to inhibit insulin signaling pathways, further contributing to insulin resistance.

Oxidative stress is another key factor in PCOS pathogenesis, as it affects ovarian steroidogenesis by increasing androgen levels and disrupting follicular development, leading to infertility. Additionally, oxidative stress has been associated with obesity, insulin resistance, and cardiovascular risks in PCOS patients. Multiple studies have shown that markers of oxidative stress-related inflammation are positively correlated with androgen levels in individuals with PCOS.

4) Symptoms of PCOS

PCOS symptoms vary from person to person and may change over time. Common symptoms include:

- Irregular Menstrual Cycles: Heavy, prolonged, intermittent, unpredictable, or absent periods
- Infertility
- Skin Issues: Acne or excessively oily skin
- Excessive Hair Growth: Unwanted hair on the face or body (hirsutism)
- Hair Loss: Thinning hair or male-pattern baldness
- Weight Gain: Particularly around the abdominal area

PCOS is also associated with a higher risk of developing:

- Type 2 Diabetes
- Hypertension (High Blood Pressure)
- High Cholesterol
- Cardiovascular Disease
- Endometrial Cancer

5) Diagnosis of PCOS

PCOS is diagnosed when at least two of the following criteria are met:

- Signs of Elevated Androgen Levels: This includes excessive facial or body hair, hair loss, acne, or high blood testosterone levels (after ruling out other causes).
- Irregular or Absent Menstrual Periods: Once other possible causes have been excluded.

- Polycystic Ovaries on Ultrasound

Doctors also consider factors such as family history, puberty, and menopause when diagnosing PCOS. Women with a family history of PCOS or type 2 diabetes have a higher risk of developing the condition.

6) Role of Caesalpinia bonducella in PCOS Treatment

Since ancient times, medicinal plants have played a vital role in human health and well-being. Herbal medicine is based on the principle that plants contain natural compounds that can improve health and treat diseases. C. bonducella has been widely studied for its medicinal properties, with most research focusing on its seeds and shells.

The seed kernel of C. bonducella is particularly valuable for treating fevers, including intermittent and chronic fevers. A traditional remedy involves mixing 15-30 grains of the kernel powder with an equal amount of black pepper and consuming it three times daily. The roasted kernel decoction is also used for asthma, while kernel extract combined with ginger, salt, and honey is given to infants with digestive issues. A paste made from the kernel is used to treat boils and swellings. Additionally, a cake made from 30 grains of powdered kernel fried in ghee is administered twice daily for conditions like acute orchitis, ovaritis, and scrofula.

VI. PHYTOCHEMISTRY OF CAESALPINIA BONDUCELLA

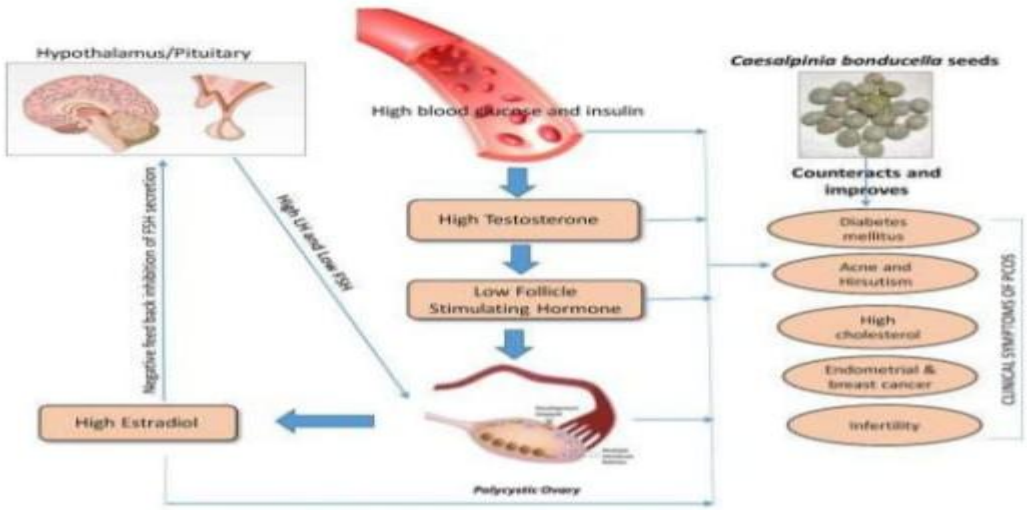
The primary alkaloid in C. bonducella is Natin, found in the shell, seed, and twigs. The seed contains Bonducin, a potent glycoside, along with saponins and terpenoids. The shell is composed of fatty oils, starch, sucrose, phytosterols, and various unsaturated acids, including stearic, palmitic, oleic, linoceric, and linolenic acids. The protein and amino acid content ranges from 7.43% to 25.35%.

Studies suggest that C. bonducella seeds possess anti-diabetic properties, making them useful for managing type 2 diabetes, a condition closely linked to PCOS. The plant extract has demonstrated anti-hyperglycemic effects by blocking glucose absorption and reducing blood urea nitrogen (BUN) levels. It also lowers LDL cholesterol levels while improving lipid profiles in diabetes-induced hyperlipidemia.

1) Scientific Studies on C. bonducella and PCOS

In 1994, Velazquez et al. reported that metformin, an insulin-sensitizing drug, improved hyperinsulinemia, insulin resistance, hyperandrogenemia, and blood pressure in PCOS patients while restoring normal menstruation and fertility. Similarly, C. bonducella has been found to alter endocrine functions by lowering estrogen levels and interfering with estrogen feedback mechanisms. Phytoestrogens present in the plant bind to estrogen receptors in the pituitary or hypothalamus, indirectly influencing ovarian steroidogenesis.

Research on Mifepristone-induced PCOS female rats has shown that ethanolic seed extracts of C. bonducella (ESECB) positively impact enzymatic and non-enzymatic antioxidant levels while reducing histopathological changes associated with PCOS. This suggests that C. bonducella could serve as a natural therapeutic option for PCOS management by regulating insulin resistance and β-cell function.



The diagram illustrates how Caesalpinia bonducella seeds help counteract the symptoms of PCOS.

a) PCOS Mechanism:

Elevated blood glucose and insulin levels contribute to increased testosterone production.This leads to a decrease in follicle-stimulating hormone (FSH), affecting ovarian function and causing polycystic ovaries.The high testosterone and altered FSH levels disrupt hormonal balance, leading to conditions such as high estradiol and a high LH/FSH ratio.

b) Effects of Caesalpinia bonducella Seeds:

The seeds help regulate hormonal imbalances and improve insulin sensitivity.They alleviate symptoms associated with PCOS, including diabetes, acne, hirsutism, high cholesterol, endometrial and breast cancer risks, and infertility.This highlights Caesalpinia bonducella's potential as a natural remedy for managing PCOS symptoms.

VII. PHYTOCHEMICAL CONSTITUENTS OF CAESALPINIA BONDUC SEEDS

The seeds of Caesalpinia bonduc contain several important phytochemicals, including bonducin (a bitter compound), phytosterin, various fatty acids, and caesalpins (α, β, γ, δ, and ψ). Additionally, newly identified constituents such as the diterpene caesalpin, the homoisoflavonebonducellin, and citrulline have been reported.The seed kernel contains cassanefurano diterpene, which exhibits strong antimalarial properties against the multidrug-resistant K1 strain of Plasmodium falciparum, along with several cassane diterpenoids. Pipataline has been isolated from the bark, while cassane diterpenes, including caesaldekarin A, have been identified in the roots. Moreover, cytotoxic flavonoids have been extracted from the young twigs and leaves.

Phytochemical Analysis

S. No.	*C. bonduc* Plant Part(s)	Name of the Chemical Constituents	References
1.	Seed Seed Kernel	Bonducin- A bitter substance Phytosterinin Fatty acids, Caesalpins (α, β, γ, δ and ψ), Bonducellin (Homois of lavone) Citrulline Cassanediterpenes, Neocaesalpins C, D Bondenolide Neocaesalpin P, Neocaesalpin H Cordylane A, CaesalpininB Bonducellpin E,	[55, 44]
		Caesalpinolide A Caesalpinolide C, D and E	[56]
		Cassane Diterpinoids	[57]
		Cassane Furanoditerpene	
2.	Bark	Caesaldekarin J Pipataline	[58]
3.	Young Twigs Leaves	Cytotoxic Flavonoids	[60]
4.	Roots	Caesaldekarin A	[59]

Fig. Phytochemical Constituents of Caesalpinia bonducella

Phytochemical screening was conducted to detect the presence of saponins, flavonoids, quinones, alkaloids, and tannins, following the method described by Maria Shabbir et al. Wagner's reagent was used to test for alkaloids, the foam test for saponins, the lead acetate test for flavonoids, Braemer's test for tannins, and the sulfuric acid test for quinones. These analyses were performed on the water extracts of both the seed and shell separately.

A. A.In-vitro Anti-inflammatory Assay

The anti-inflammatory activity was assessed using the method of Gandhisan et al. Blood was collected from healthy volunteers and mixed with an equal volume of Alsever's solution (containing 2% dextrose, 0.8% sodium citrate, 0.5% citric acid, and 0.42% NaCl). After centrifugation at 3,000 rpm, the cells were washed with saline.

Extracts at concentrations of 200, 400, 600, 800, and 1000 µg/ml were prepared in distilled water. Each extract (1 ml) was combined with 1 ml of phosphate buffer, 2 ml of hypo-saline, and 0.5 ml of HRBC suspension.

The mixture was incubated at 37°C for 30 minutes, followed by centrifugation at 3,000 rpm for 20 minutes. The HRBC membrane stabilization (protection) was calculated using the formula:

$$\% \text{ Protection} = 100 - \left(\frac{\text{Optical density of treated sample}}{\text{Optical density of control}} \right) \times 100$$

Aspirin (1 mg/ml) served as the reference standard.

B. Anti-Diabetic Assay

For anti-diabetic activity, 100 µl of plant extract at 500 and 1000 µg/ml was incubated with 200 µl of amylase at 37°C for 20 minutes. Then, 100 µl of 1% starch solution was added, and the mixture was further incubated at 37°C for 10 minutes. The reaction was stopped by adding 200 µl of DNSA reagent, followed by heating in a boiling water bath for 5 minutes. The reaction mixture was diluted with 2.2 ml of water, and absorbance was measured at 540 nm against a blank.

C. Determination of DPPH Free Radical Scavenging Activity

Antioxidant activity was evaluated using ascorbic acid as the standard and DPPH (1,1-diphenyl-2-picrylhydrazyl) as the control. 100 µl of extract was mixed with 3 ml of DPPH solution and incubated for 30 minutes. Absorbance was measured at 517 nm, and free radical scavenging ability was determined using the equation:

$$\% \text{ DPPH Scavenged} = \left(\frac{A_c - A_t}{A_c} \right) \times 100$$

where Ac is the absorbance of the control reaction, and At is the absorbance in the presence of the extract. The antioxidant potential was expressed as IC50, which represents the concentration of dry material (mg/ml) required to inhibit 50% of DPPH radicals. Each value was derived from the regression equation.

D. Anti-Mitotic Activity

The anti-mitotic activity was evaluated using green gram seeds of equal weight. The seeds were germinated in 500 µl of plant extract at concentrations of 10, 20, 30, and 40 mg/ml in a 24-well microtiter plate. Seeds germinated in distilled water served as the control, while doxorubicin was used as the standard (as per Kumar and Singhal, 2009). The morphological study was based on radicle length, and the experiment was performed in triplicates.

E. AntimicrobialActivity

The antimicrobial properties of the extract were tested against Staphylococcus aureus, Candida albicans, and Mycobacterium smegmatis using the agar diffusion method. 30 ml of nutrient agar was poured into petri plates containing 100 µl of microorganisms (McFarland's standard No. 5). After 24 hours, the zone of inhibition was measured and compared with the standards Streptomycin (for bacteria) and Candid B (for fungi).

VIII. RESULTS

A. Phytochemical Analysis

Qualitative analysis confirmed the presence of secondary metabolites such as tannins, flavonoids, and alkaloids in the water extract of C. bonducella. Both the seed and shell contained flavonoids and alkaloids, while saponins were abundant in both parts, indicating their potential therapeutic benefits.

B. In-vitro Anti-inflammatory Activity

The HRBC membrane stabilization method was employed to assess anti-inflammatory activity. The ability to prevent hypotonicity-induced HRBC membrane lysis was used as an indicator of the extract's anti-inflammatory potential.i

Table 1: Phytochemical analysis of water extract of seed and shell. '+' indicates the presence of the metabolites and '-'indicates the absence the metabolites. '+++' indicates higher concentration of metabolites.

	Aqueous Extract	
	Seed	Shell
Tannins	-	-
Flavanoids	+	+
Alkaloids	+	+
Saponins	+++	++
Coumarins	-	-
Quinones	-	-
Phenols	-	-

Table 2: *In vitro* **Anti- inflammatory activity of** *C. bonducella* **aqueous extract.**

% Protection	200 µg/ml	400 µg/ml	600 µg/ml	800 µg/ml	1000 µg/ml
Seed	44.927 ± 4.03	72.463 ± 2.366	73.913 ± 4.81	82.608 ± 4.098	84.37 ±2.19
Shell	56.521 ± 6.072	63.768± 1.366	72.463 ±3.414	86.956 ± 3.56	91.304± 4.054
Aspirin	76.811 ± 0.682	79.71 ± 1.18	86.956 ± 4.381	88.405± 4.782	95.652 ± 4.652

Table 3: Inhibition of α-amylase by aqueous extract of *C. bonducella*.

% Inhibition	500µg/ml	1000µg/ml
Shell	31.818%	78.947%
Seed	-	47.36%
Glycomet GP2(Standard drug)	59.20%	80.97%

Table 4: % antiradical activity of *C. bonducella* **aqueous extract.**

% Anti -radical activity	200 µg/ml	400 µg/ml	600 µg/ml	800 µg/ml	1000 µg/ml
Shell (in %)	41.17 ± 6.355	55.88 ± 1.385	58.82 ± 1.3	61.76 ± 1.385	61.76 ± 1.385
Seed (in %)	-	-	-	-	-
Standard (in %)	74.28 ±	80 ±	85.71 ±	87.14 ±	88.571 ±

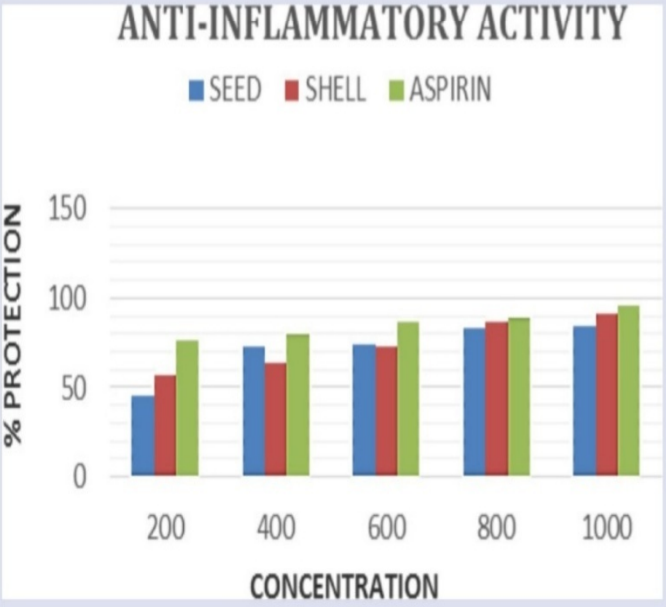


Figure 1: *In-vitro* Anti- inflammatory activity of *C. bonducella* aqueous extract.
(source: Personal collection)

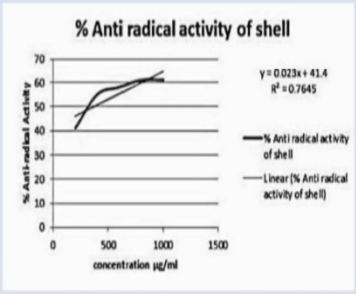


Figure 2: IC_{50} value of the aqueous extract of shell. The IC_{50} was found to be 350.638 µg/ml for the shell extract.
(source: Personal collection)

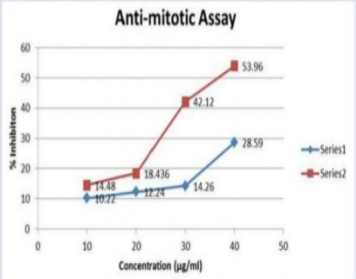


Figure 4: Antimitotic assay for *C. bonducella* aqueous extract.
(source: Personal collection)

Fig. Results of Phytochemical Analysis of Caesalpinia bonducella

IX. OTHER PHARMACOLOGICAL ACTIONS

The following table shows the Pharmacological studies of Caesalpinia bonducella:-

S. No.	Activity	Part/ extract/	Experimental Studies/Cell Lines/ Animal Model/ microorganism
1	Antidiabetic	Alcoholic Extract- Seed Polyphenol Extract	Alloxan Induced Diabetic Male Albino Rats [14] Different doses of extract to hyperglycemic rats restored blood and serum glucose, insulin, reduced oxidative stress in pancreatic β cells by restoring free radical scavenging potential [15]
		Seed and shell Extract	*in-vitro* [16]
		Seed Extract	Showed a significant Antidiabetic activity in alloxan induced hyperglycemiain rats [17]
		Aqueous and Ethanolic Extracts -Seeds	Significant blood sugar lowering effecting both type 1 and 2 diabetes mellitus in Long Evans rats [18]
2	Anti-inflammatory Antipyretic and Analgesic	Seed Oil	The oil exhibited anti-inflammatory activity in experimental rats in a paw edema test induced by carrageenan [19]
		Ethanolic extract of whole seeds	In experimental albino rats [39]
		Ethanolic extract (70%) of seed kernel	Exhibited marked antipyretic activity against Brewer's yeast- induced pyrexia in rats, significant central analgesic activity and peripheral analgesic effect in both mice and rats In adult albino rats or mice [40]
		Flower extract	Reduced pyrexia in adult mice in carrageenan-induced inflammation, cotton pellet induced chronic granulomatous inflammation and autacoids-induced inflammation [41]
3	Antibacterial Antibacterial and Cytotoxic activities	Methanolic Seed extract	Inhibited growth of Gram-positive and Gram-negative bacteria by the diffusion method and exhibited a similar activity of the standard antibacterial kanamycin [42]
		Methanol extract and fractions of leaves	The extracts showed different zones of inhibition against four gram-positive and five gram-negative bacteria [43]
		Methanolic leaf and Bark extracts	Gram positive and Gram negative bacteria [44]
4	Anti-cancer	Phytochemicals from young twigs and leaves	*In silico* interaction between phytochemicals and cancer target proteins (TK, VEGF, and MMP) compared with their respective drug inhibitors [45]
5	Anticonvulsive	Petroleum Ether	Exhibited activities in convulsions models [46]
6	Antioxidant	Ethanolic extract	*in vitro*-showed a high free radical-scavenging activity [47]
		Chloroform Extract	Exhibited *in vitro* radical scavenging effect [48]
7	Anti-filarial	crude extract or fractions of the seed kernel	Exhibited gradual fall in microfilariae count in *L. sigmodontis*-cotton rat model [49]
8	Anti-malarial	Aqueous, cold alcoholic and hot alcoholic extracts	Exhibited inhibition in growth of *Plasmodium falciparum* [50]
		Root Extract	Exhibited dose-dependent suppression of parasite growth *in vivo* in mice [51]
9	Anti-Tumour	Methanol extract	Exhibited significant antitumor activity in Ehrlich ascites carcinoma (EAC)-bearing Swiss albino mice [52]
10	Immunomodulatory	Ethanolic Seed Extract	*in vivo* experiments- sheep red blood cell and rats [53]
		Aqueous Seed extract	*in vivo* ,cell mediated and humoral components of the immune system in rats [54]

A. Anticancer Activity

The antidiabetic properties of ethanol and aqueous seed extracts of Caesalpinia crista were assessed in streptozotocin-induced diabetic mice. Both extracts demonstrated antidiabetic effects, leading to a notable reduction in serum glucose, cholesterol, and triglyceride levels compared to the untreated diabetic group after three weeks of treatment.

B. Anticonvulsant Effects

The anticonvulsant potential of Caesalpinia crista seed extract was evaluated using models of pentylenetetrazole-, maximal electroshock-, strychnine-, and picrotoxin-induced convulsions. Diazepam was used as the reference standard for all models except the maximal electroshock model, where phenytoin served as the standard. The seed kernels were powdered and extracted successively with petroleum ether, ethanol, methanol, and water. These extracts were then administered as a suspension in 2% gum acacia. In the convulsion models, the medium (600 mg/kg) and high doses (800 mg/kg) of the extract exhibited significant anticonvulsant activity.

C. Antidiarrheal Effects

The antidiarrheal activity of C. crista methanolic leaf extract fractions was tested at two doses (200 mg and 400 mg) using a castor oil-induced diarrhea model in rats. The results were compared with loperamide. All fractions displayed a dose-dependent antidiarrheal effect, with the ethyl acetate fraction showing the highest inhibition of defecation (51.11%), while loperamide exhibited a 57.75% inhibition rate.

D. Antioxidant Action

The antioxidant properties of C. crista leaf and seed extracts were investigated. The 70% methanol leaf extract was analyzed for its phenolic content and antioxidant activity (Mandal et al., 2011). The total phenolic content was recorded at 50 mg GAE/ml, while the total flavonoid content was 107 QE/ml. The total antioxidant activity, measured using trolox equivalent antioxidant capacity (TEAC), was 0.6. The IC50 values for scavenging various reactive oxygen species (ROS) were:

0.4 µg/ml for hydroxyl radicals
25 µg/ml for superoxide radicals
34 µg/ml for nitric oxide
61 µg/ml for singlet oxygen
170 µg/ml for hypochlorous acid

For in vivo studies, oral administration of the leaf extract to normal mice for a week led to a significant increase in the activity of antioxidant enzymes.

X. PHYSIOCHEMICAL PROPERTIES

SL No.	Quantitative Standards	Seed Kernels (% w/w)	Seed Coat (% w/w)
1	Loss on drying	10.22	10.06
2	*Extractives:*	52.00	36.20
	a) Water	21.44	14.64
	soluble	44.80	03.36
	b) Alcohol soluble		
	c) Pet. ether		
3	*Ash values:*	2.60	3.40
	a) Total ash	1.56	1.94
	b) Acid-insoluble ash	0.87	1.07
	c) Water-soluble ash		

XI. ANALYTICAL VALUES

Acid value	4.71
Saponification value	144.46
Ester value	139.75

XII. USE IN AYURVEDIC MEDICINE

1) Rasa (Taste): Bitter (Tikta) and Astringent (Kashaya)
2) Veerya (Potency): Hot (Ushna)
3) Dosha Effect: Balances all three doshas (Tridosha)
4) Vipak (Post-digestive Effect): Pungent (Katu), balances Kapha and Vata, reduces swelling (Sotha Har), strengthens the body (Badana Sthapan), aids digestion (Dipan), promotes bowel movement (Anuloman), relieves respiratory issues (Swashar), acts as a diuretic (Mutral), and reduces fever (Jwaraghan).

XIII. MODERN USES

1) The biological activities and medicinal properties of Caesalpinia bonducella are detailed in Table 3.
2) The powdered form of C. bonducella is listed in the Indian Pharmaceutical Codex, with a recommended dose of 15-18 grains.
3) It is known to induce perspiration, helping reduce fever.
4) A combination of kernel powder, sugar, and goat milk is beneficial for liver disorders.

XIV. NUTRITIONAL VALUE

C. bonducella has been found to contain various nutrients in significant amounts. It includes crude fiber (12.79–14.07%), protein (18.65–20.32%), fat (6.54–7.23%), and carbohydrates (16.91–18.56%). Its caloric value ranges between 376.27 and 402.12 Kcal per 100 grams. The plant also provides essential minerals such as calcium (0.150–0.184%), phosphorus (0.17–0.22%), sodium (0.07–0.08%), and iron (0.22–0.5%). Additionally, it offers vitamin C (0.016–0.043 IU/g) and vitamin A (416.75–700.14 IU/g).

The seeds specifically provide an energy value of 73.6%, crude fiber (3.3 mg/g), total fat (3.6%), free amino acids (1.82%), protein (17.6%), and carbohydrates (18.4%). They also contain free fatty acids (0.03 mg/g), vitamin E (6.09 µg/g), vitamin C (4.2 µg/g), thiamine (10.6 µg/g), niacin (22.6 µg/g), riboflavin (89.6 µg/g), and cellulose (2.59 mg/g).

Analysis through XRF and flame photometry revealed that the plant is rich in minerals such as potassium (K), calcium (Ca), iron (Fe), phosphorus (P), sulfur (S), magnesium (Mg), silicon (Si), chlorine (Cl), lead (Pb), palladium (Pd), aluminum (Al), molybdenum (Mo), copper (Cu), and zinc (Zn).

The seeds also contain enzymes like lipase (12.9 µg/g), amylase (12.3 µg/g), catalase (9.6 µg/g), alkaline phosphatase (0.56 µg/g), and acid phosphatase (0.25 µg/g).

XV. CONCLUSION

The significant nutraceutical potential of this plant, owing to its effectiveness and versatility, highlights the need for further in-depth research. Acute toxicity studies have confirmed its safety for human consumption, making it suitable for use in commercial nutraceutical formulations. Additionally, the plant exhibits a range of pharmacological effects across various diseases and conditions, establishing it as a valuable asset for the Indian nutraceutical industry.

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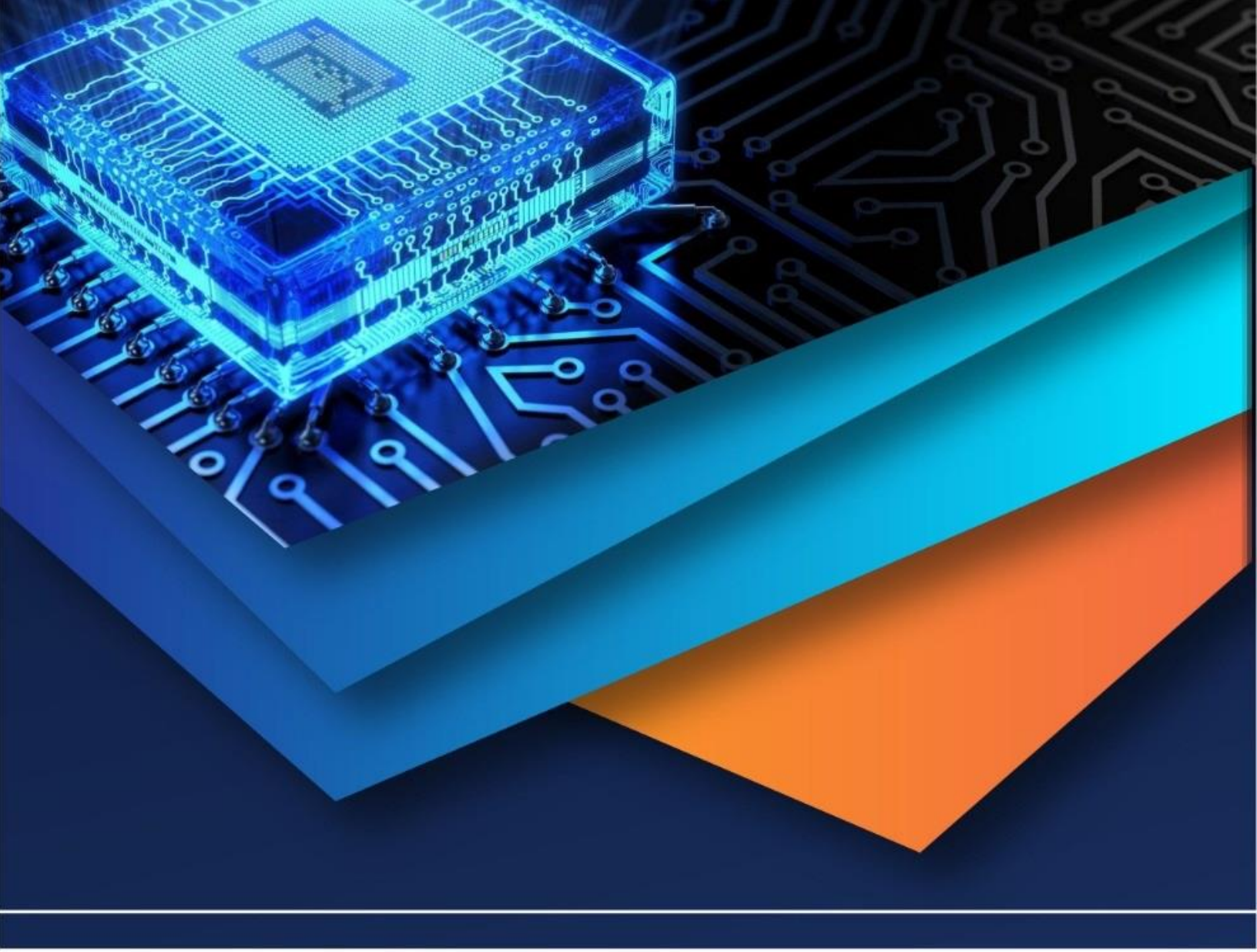

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