



THE ROLE OF PHENOL AND FLAVONOID IN THE SYNTHESIS AND APPLICATION OF NANO GRAPHENE OXIDE

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ABSTRACT: *The unique properties of graphene oxide have generated significant interest in recent years. Many potent aromatic drugs are water-insoluble, complicating their administration. Nano graphene oxide, a potential drug carrier, is typically synthesized through environmentally harmful chemical methods. This review emphasizes the need for more sustainable approaches to address these challenges while maintaining graphene oxide's effectiveness in drug delivery. Plant extracts are rich in bioactive compounds known as phytochemicals which have the ability to synthesize nano graphene oxide. A large and most intricate class of these phytochemicals are Phenolic compounds which have an aromatic ring and one or more hydroxyl groups in their structural conformations. Based on their structural composition, they are divided into subgroups that include phenolic acids, flavonoids, tannins, coumarins, lignans, quinones, stilbenes, and carotenoids. Plant polyphenols are gaining increasing attention because of their potent antioxidant properties and important roles in preventing oxidative stress-related diseases. The extraction, identification, and characterization of phenolic compounds from a range of plant sources has become a major area of study in the health and medical fields in recent years. The role of phenol and flavonoid in the synthesis and application of nano composites are also covered in this review.*

KEYWORDS: Phenolic compound, Nano graphene oxide, flavonoids, antioxidant, phytochemicals, health benefits, Phytochemicals.



INTRODUCTION

Graphene, often hailed as a “material of the future,” is one of the most extensively studied materials due to its unique properties (Rümmeli et al., 2011). It is composed of a single layer of carbon atoms arranged in a honeycomb lattice with sp^2 hybridized orbitals (Yang et al. 2018). These remarkable characteristics make graphene highly promising for a wide range of applications, including field-effect transistors (FETs), sensors for gases and biomolecules, transparent conductive films (TCFs), and advanced batteries (Jiríčková et al., 2022).

One of the most significant graphene derivatives, graphene oxide, is also gaining a lot of attention as a membrane material because of its many oxygen-containing functional groups (such as hydroxyl, epoxy, carbonyl, and carboxyl groups) on the basal plane and at the edges (Aliyev et al., 2019). These groups promote good dispersity in water and ease of functionalization and crosslinking under the right circumstances (Bashir et al., 2020). Graphene oxide can be produced from graphite in vast amounts by oxidation and exfoliation; the Brodie, Staudenmaier, Hofmann, and Hummers processes have all been applied to the synthesis of graphene oxide (Jiríčková et al., 2022). All four of these techniques entail oxidizing graphite in the presence of strong acids and oxidants. By varying the precursor graphite and the reaction conditions, different oxidation levels can be achieved.

Reviewing these four techniques, the Hummers method is the most widely used and well-liked approach today, requiring just slight modifications to synthesize graphene oxide for a variety of uses (Anegebe et al., 2024). Flake graphite is treated using a combination of potassium permanganate, sulfuric acid, and sodium nitrate; the usage of sodium nitrate produces harmful gasses like NO_2/N_2O_4 . Recently, potassium permanganate, concentrated sulfuric acid, and phosphoric acid were combined in an oxidation combination to create Tour's technique, which prevents the release of harmful gasses. This process can provide high-yield, highly oxidized hydrophilic graphene oxide. Higher oxidation levels in graphene oxide are associated with more persistent damage (Pizzino et al., 2017). Low reaction temperature was discovered by Eigler et al., (2013) to enhance graphene oxide quality (Singh et al., 2016).

Brodie was the first to use $KClO_3$ in a harsh fuming HNO_3 reaction to create a novel hydrogen, carbon, and oxygen compound (Aafreen et al., 2024). The quality of flake graphite has increased as a result of this groundbreaking effort. After washing the batch to get rid of any salts that had formed throughout the process, he dried it at $100\text{ }^\circ\text{C}$ and put it back in the oxidizing atmosphere. A material with a "light yellow color" that remained unchanged after further oxidation treatment was created after three iterations of that technique. He determined the final molecular formula of the oxidized graphite to be $C_{11}H_4O_5$, based on the elemental analysis of his product. In addition, he discovered that the substance dispersed in basic or pure water but precipitated in acidic environments. For these reasons, he named the recently created compound "graphic acid." The material's C:H:O composition changed to 80.13:0.58:19.29 after heating to $220\text{ }^\circ\text{C}$ due to the reduction of carbonic acid and carbonic oxide. Nevertheless, the lengthy reaction time and dangerous gas emissions of this method restrict its application, even though it has the potential to oxidize graphite (Fan et al., 2018).

Using an excess of the oxidizing agent and concentrated sulfuric acid as an additional additive, L. Staudenmaier improved on Brodie's work in 1898 (Panicker et al., 2021). He enhances Brodie's $KClO_3$ -fuming HNO_3 preparation by (i) increasing the acidity of the mixture by adding concentrated sulfuric acid (H_2SO_4) and (ii) adding multiple aliquots of potassium



chlorate solution during the reaction. These modifications made it possible to produce highly oxidized graphite oxide in a single reaction vessel, which made the synthesis of graphene oxide simpler. The overall degree of oxidation produced by this small modification to the synthesis process was comparable to Brodie's multiple oxidation method (C: O ~ 2: 1). But the process of preparing Staudenmaier's mixture required a lot of time and care; adding potassium chlorate usually took more than a week, and an inert gas was required to remove the chlorine dioxide that developed. Additionally, there was always a risk of explosion. As a result, research was still being done on how to improve the new oxidation process. Several other groups have also employed this technique, along with a modified version, to synthesize graphite oxide (Lojka et al., 2019).

Hofmann et al., (2012) prepared graphite oxide by oxidizing graphite and combining concentrated sulfuric acid, concentrated nitric acid, and KClO_3 (Hu & Gao, 2023). In addition to oxidizing the graphite powder in an acidic solution, KClO_3 is a very potent oxidizing agent that frequently serves as an *in-situ* source of dioxygen, which is the reactive species. Numerous research teams have used the Hofmann method to synthesize graphene oxide for various application purposes such as solar cells, field-effect transistors, and gas sensors (Marcano et al., 2010).

A different way to oxidize graphite was demonstrated by Hummers and Offeman in 1958. They did this by reacting graphite powder with a combination of concentrated H_2SO_4 , NaNO_3 , and KMnO_4 . First, 2.3 liters of sulfuric acid were mixed with 100 grams of graphite powder and 50 grams of sodium nitrate. The mixture was then cooled to 0 degrees Celsius using an ice bath. Next, 300 g of potassium permanganate were added to the suspension. After being stirred until the suspension thickens, the mixture is further diluted with hot water and treated with 3% H_2O_2 to convert any remaining permanganate and manganese dioxide to colorless soluble manganese sulfate. In order to eliminate the soluble mellitic acid salt, the diluted suspension was lastly filtered and repeatedly cleaned with warm water. By centrifuging and then dehydrating at 40°C over phosphorus pentoxide in vacuum, graphitic oxide was obtained in its dry form. For the synthesis of graphite oxide, a number of research teams have recently turned to Hummers enhanced method (Qiu et al., 2017).

Marcano et al., (2010), reported an enhanced process for the preparation of graphite oxide. Through the use of KMnO_4 in greater quantities and a 9:1 mixture of H_2SO_4 and H_3PO_4 , the oxidation process was improved in this new procedure by eliminating NaNO_3 . By comparison with Hummers' method, this improved oxidation method yields more graphite oxide and increases the efficiency of graphite oxidation to a large degree. Additionally, this oxidation method stopped the production of harmful gases (like NO_2 and N_2O_4) (Feicht et al., 2019).

Issues with Current Synthesis Methods

The synthesis described above employs chemical processes, yet it faces several issues:

- i. **Low Throughput:** Liquid phase exfoliation results in low throughput.
- ii. **Structural and Manufacturing Flaws:** Graphene produced may exhibit certain structural and manufacturing flaws, making it impossible to guarantee purity.
- iii. **Impurities:** Unwashed salt impurities found between graphene layers in the electrochemical method affect graphene's conductivity.



- iv. **Control of Thickness Parameter:** The thickness parameter cannot be controlled as precisely as with the CVD method or epitaxial graphene growth process (Kiciński & Dyjak, 2020).

Therefore, a better approach is required to address the aforementioned issues. Plant extracts were utilized as a solution to these issues. Plant extracts have the ability to synthesize nanographene oxide and contain phytochemicals.

Phytochemicals in Plant Extracts

Phytochemicals are plant-based bioactive compounds produced by plants for their protection (Kumar et al., 2023). Over a thousand phytochemicals have been identified to date, and they can be obtained from a variety of foods, including whole grains, fruits, vegetables, nuts, and herbs (Kumar et al., 2023). A few noteworthy phytochemicals are dietary fibers, specific polysaccharides, carotenoids, polyphenols, isoprenoids, phytosterols, and saponins. These phytochemicals have antiviral, antibacterial, antidiarrheal, anthelmintic, antiallergic, and strong antioxidant properties (Pawase et al., 2024). In addition, they support immunity, gap junction communication, gene transcription regulation, and protection against lung and prostate cancers (Oliveira et al., 2022).

The affinity of phytochemicals for solvents and their heat tolerance varies. The choice of solvent has an impact on the quality of the recovered phytochemical and its use in the production of food and nutraceutical products. The solvents are classified as green solvents (water, ethanol, glycerol, fatty acids/oils, acetic acid, ionic liquids, carbon dioxide (CO₂), deep eutectic solvents and natural deep eutectic solvents (NADES), etc.) and other solvents like acetone, chloroform, butanol, methanol, ethyl acetate, methyl acetate, benzene, hexane, etc. (Kumar et al., 2023).

A few significant categories of secondary metabolites are:

Plants produce chemicals known as secondary metabolites (phytochemicals), are organic compounds that do not play a direct role in the usual processes of growth, development, or reproduction in an organism. Their roles are yet to be known in growth, photosynthesis, reproduction, and other primary processes.

These phytochemicals will be arranged according to certain attributes, such as their origin in biosynthesis, shared structural features, and solubility characteristics.

Compounds containing nitrogen and/or sulfur in their structure; they are soluble and have a variety of biosynthetic sources, but they are primarily derived from amino acids. An example of these compounds are nitrogen compounds called cyanogenic glycosides, which break down when a plant is crushed and release volatile, toxic substances like hydrogen cyanide (HCN). These compounds are not toxic on their own. Amygdalin is one such instance.

Terpenoids, depending on the class, are liposoluble, structurally based on the isoprene molecule, and biosynthetically linked to either the glyceraldehyde phosphate-pyruvic acid pathway or the mevalonic acid pathway (Mendoza & Silva, 2018).

Polyphenols, also known as polyhydroxyphenols, belong to a structural class of compounds primarily made up of naturally occurring substances, though they can occasionally be artificial



or semi-artificial. Polyphenols are named for their several phenolic structural units and are divided into groups such as phenolics, stilbenes, flavonoids, tannins, and lignin.

As one of the most extensively researched classes of phytochemicals, polyphenols are primarily derived from plants. These phytochemicals are widely distributed throughout the plant kingdom and are present in a variety of fruits, drinks, foods, and other items that form part of the human diet. They are compounds with high nutraceutical values that possess antioxidant, anti-inflammatory, and antimicrobial properties. They also have blood pressure-lowering, skin-protecting, cardioprotective, and anticancer properties.

Flavonoids and other phenolic compounds are commonly referred to as secondary metabolites of plants that contain an aromatic ring with at least one hydroxyl group. Over 8000 phenolic compounds have been reported as naturally occurring substances from plants. Interestingly, half of these phenolic compounds are flavonoids, which present as aglycone, glycosides, and methylated derivatives. The majority of the secondary metabolites of spices and herbs are useful in pharmaceutical products and have a significant market share. These secondary metabolites are the most significant classes of bioactive substances found in plants (Kim et al., 2003). These phytochemical substances are found in nutrients and herbal medicines. Both flavonoids and many other phenolic components have been reported to possess potent antioxidant properties, as well as anticancer, antibacterial, cardioprotective, anti-inflammation, immune system-promoting, anti-aging, skin protection from UV radiation, and intriguing candidate for pharmaceutical and medical use (Tungmunnithum et al., 2018).

These two phytochemicals, flavonoids and phenols, have been linked to the production of nano graphene oxide (nGO) (Zhang et al., 2022). Numerous industries, including electronics, aerospace, energy, agriculture, cosmetics, medicine, and textile manufacturing, use nanoparticles extensively. They are currently employed to administer drugs, proteins, genes, vaccines, polypeptides, and nucleic acids.

The International Organization for Standardization defines a nanomaterial as a material with at least one external dimension at the nanoscale, or with an internal or surface structure ranging from approximately 1 to 100 nm. For over 150 years, graphene oxide (GO) has been recognized as a nanomaterial with numerous applications. GO is a precursor to graphene, one of the superior two-dimensional materials among the carbon allotropes (Rhazouani et al., 2021).

Particle Size Distribution and Phytochemical Effects

Polyphenol, flavonoid, and saponin extracts from *Calotropis procera* leaves were studied concerning particle size distribution (Liu et al., 2018). The extraction process for these compounds followed the guidelines provided by Latif et al. (2018) and Moustafa et al. (2010). Subsequently, the synthesis of magnetite was carried out using these phytochemical extracts instead of the aqueous leaf extract, as directed by Altemimi et al. (2017).

The specific effects of a few phytochemicals that were isolated from *Calotropis procera* leaves on the synthesis of magnetite and the distribution of particle sizes has been calculated. According to the findings, the average particle size of the magnetite synthesized from the phenol extract was 62.83 nm with a PDI (polydispersity index) of 0.241. In contrast, the flavonoid extract yielded magnetite with an average particle size of 68.02 nm and a PDI of 0.186. This indicates that while the average particle size of the flavonoid-synthesized magnetite was slightly larger, its lower PDI suggests a more controlled synthesis with a uniform size



distribution. Conversely, the saponin extract produced magnetite with a PDI of 0.323 and an average particle size of 134 nm, which is larger than the nanoscale. Generally, various mechanisms have been proposed for the synthesis of nanoparticles by different flavonoids and phenolic compounds (Aziz et al., 2021).

Certain phytochemicals extracted from the extracts have been reported to be used directly in the synthesis of nanoparticles. A study utilizing phenolic extracts from various plants to synthesize iron oxide nanoparticles has been published (Nahari et al., 2022). The study found that the particle size distribution was influenced by the types and structures of phenolic compounds. With an average particle size of 31.24 nm, zinc oxide nanoparticles were synthesized using flavonoid (quercetin) isolated from *Combretum ovalifolium* (Jeyaleela et al., 2020), while silver nanoparticles with particle sizes ranging from 5 to 80 nm were synthesized using flavonoid extracts from citrus plants (Khane et al., 2022). The findings demonstrated that while the extracts of phenol and flavonoids from *Calotropis procera* were able to synthesize magnetite on their own, the synthesis that used the entire leaf extract produced much smaller particle sizes (11.1 nm) and PDI (Kalu et al., 2022).

Plant extracts serve as reducing and stabilizing agents during the nanoparticle synthesis process (Bao et al., 2021). Though the process of bio reduction is complex, it is believed that plant extracts include naturally occurring compounds that work in conjunction with reducing agents to promote the process. Potential players in the biochemical cascades leading to the biosynthesis of noble metal nanoparticles include proteins, carbohydrates, flavonoids, and other molecules (Tungmunnithum et al., 2018).

Plants are a great option for the large-scale synthesis of nanoparticles because they are easily accessible, safe to handle, and contain a wide range of metabolites that may aid in reduction (kazemi et al., 2023).

The total phenolic and flavonoid contents of the extract were assessed in another study to identify the potent compounds responsible for the reduction of silver ions to Ag NPs. The aqueous extract of *L. nobilis* leaves was utilized to prepare Ag NPs in a simple, rapid, efficient, and sustainable way. The radical scavenging ability of both the extract and the synthesized Ag NPs was also examined. Notably, the eco-friendly synthesis of Ag NPs using *L. nobilis* extract had not been previously reported (Flieger et al., 2021).

It is suggested that a variety of biomolecules found in aqueous plant extracts, including proteins, polyphenols, and polysaccharides, may play a part in the formation of Ag NPs (Flieger et al., 2021). Researchers have screened *Laurus nobilis* (Bay) in the past for chemical components and biological activity. Extracts of *L. nobilis* were used to separate phenolic compounds, which were then assessed for use as natural antioxidants (Awada et al., 2023). *L. nobilis* aqueous extract was used to create gold nanoparticles at room temperature, and the antimicrobial activity of the extract was also assessed. They stated that, when compared to the two other species examined in the study, high yields of polyphenols were obtained from *L. nobilis* after two hours of extraction by reflux-heat using aqueous ethanol at a concentration of 35%. Four phenolic compounds were identified in the *L. nobilis* extract by HPLC analysis, and the plant had a higher concentration of phenolic compounds than two other species (Baek & Patra, 2015). A few studies have been published in the literature that demonstrate the correlation between the potency of green Ag NP synthesis and its phenolic content. *Shorea roxburghii* stem bark extract has been shown by Subramanian et al. (2013) to contain a high



concentration of total phenolic compounds, and the plant extract may be utilized as a green reducing agent for the synthesis of Ag NPs (Ahn & Park, 2020). The plants' ability to reduce was arranged in a manner consistent with their phenolic content and antioxidant potential (Ghosh et al., 2021). Begum and colleagues conducted kinetic studies utilizing FTIR and Cyclic Voltammetry, and their findings suggested that the Ag and Au nanoparticles formed were caused by the polyphenols or flavonoids found in tea leaves (Adeyemi et al., 2022). The phenolic compounds in pineapple, according to Ahmad et al., (2019), show good antioxidant activity, making these natural antioxidants a viable option for the synthesis of Ag Nps.

An assessment of the antioxidant status was conducted on the phenolic extracts of *L. nobilis*, which are well-known for their therapeutic benefits in indigenous Arab medicine. It was reported that the extract's estimated total phenol content as determined by the Folin-Ciocalteu procedure, showed a content of total phenols, flavonols, and flavones (25.70 ± 0.86 mg GAE g^{-1} dw and 12.11 ± 0.43 mg CE g^{-1} dw, respectively), which were higher than those previously found in this plant, which showed 20.94 ± 0.97 mg GAE g^{-1} dw. of total phenolic and 8.2 ± 0.21 mg CE g^{-1} dw at flavonoids (Fidan et al., 2019).

Table 1: Total Phenol and Flavonoid Content of *L. nobilis* using the Folin-Ciocalteu Procedure (Guenane et al., 2016)

Plant	Total phenol (Folin) (mg GAE g^{-1} dw)	Flavonols and Flavones (mg CE g^{-1} dw)
<i>L. nobilis</i> extract	$25.70 \pm 0.86^{\dagger}$	12.11 ± 0.43

[†]Data are presented as mean \pm standard deviation (S.D.) of n = 3.

The major contribution of polyphenolic compounds to the synthesis of AuNPs was revealed by pyrolysis-gas chromatography-mass spectrometry, and this was further supported by the reduction of total phenolic and total flavonoid contents within 60 minutes, from 48.08 ± 1.98 to 9.59 ± 0.92 mg GAE/g and 32.02 ± 1.31 to 13.8 ± 0.97 mg CE/g, respectively.

Reaction mechanism provided an explanation for the roles played by flavonoids and phenolic compounds in the production of spherical-shaped AuNPs based on experimental results (Ahmad et al., 2019).

The total phenolic and flavonoid contents of the *L. nobilis* leaf aqueous extract were assessed, according to Sulaiman, and Balachandran (2012). The plant is abundant in flavonoids (21.576 ± 0.0763 mg/L; 2.049 ± 0.0031 mg/g) and phenolic compounds (23.964 ± 0.0698 mg/L; 2.272 ± 0.0028 mg/g), according to the results. These are displayed in the table below.

Table 2: The Total Phenolic and Flavonoid Contents of the *L. nobilis* Leaf Aqueous Extract (Sulaiman and Balachandran, 2012)

Plant	Total Phenol (mg/L)	Flavonoids (mg/L)
<i>L. nobilis</i> extract	23.964 ± 0.0698	21.576 ± 0.0763
<i>L. nobilis</i> extract	2.272 ± 0.0028	2.049 ± 0.0031

The phytochemical content of *Calotropis procera* observed in a study agrees with other reports which showed the presence of phenols, alkaloids, tannins, flavonoids and saponins. Similar values for the total content of some of the phytochemicals have also been reported; Banerjee et al., (2020) reported a total phenol content of 40.7 (mg GAE g^{-1}) while Najjar et al., (2016)

recorded a total flavonoid content of 36.75 (mg GAE g⁻¹). Manal and Amal, (2018), however reported higher values, with a total phenol and flavonoid content being 56.3 (mg GAE g⁻¹) and 41.4 (mg QE g⁻¹) respectively. Variation in the phytochemical content could be attributed to agro-climatic factors in the environment where the plant was collected from. The result therefore establishes that *Calotropis procera* contains important phytochemicals that can be involved in the reduction, stabilization and capping processes during magnetite synthesis.

Recently, polyphenols have received the attention of scientists and consumers, due to their potential medicinal properties in the prevention and cure of various degenerative diseases, particularly cancers, cardiovascular diseases and neurodegenerative diseases (Pandey & Rizvi, 2009).

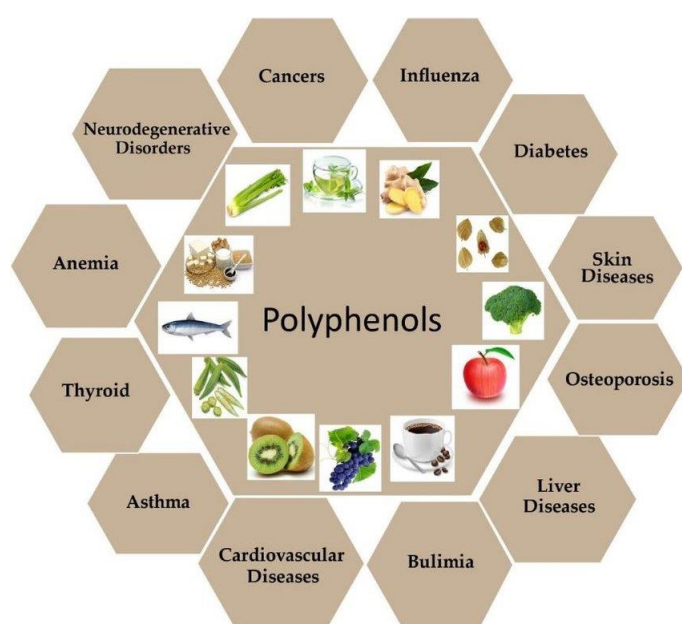


Figure 1: Health Benefits Effect of Dietary Polyphenols. Polyphenols are largely found in fruits, vegetables, spices, and beverages. Most of these compounds are involved in protection against the development of chronic diseases such as cardiovascular diseases (CVDs), neurodegenerative diseases, cancer, diabetes, osteoporosis, and liver diseases.

THE ROLE OF PHENOL IN THE SYNTHESIS OF GRAPHENE OXIDE

Phenolic compounds are among the possible pollutants that impact natural aquatic systems. Phenolic acids, flavonoids, tannins, and stilbenes are examples of phenolic compounds. They are used in agriculture and are present in many industrial processes, such as pulp and paper, synthesis of pharmaceuticals, oil refining, production of polymers and resins, and food processing (H. Fini et al., 2022). As a result, phenols are now often found in wastewater and in natural water.

The US Environmental Protection Agency (USEPA), the National Pollutant Release Inventory (NPRI) of Canada and the European Union (EU) consider phenols and their derivatives as priority pollutants, due to their serious impact on humans, animals and the aquatic environment



(Mohd, 2020). Therefore, wastewater treatment plants are requested to decrease the concentration of those compounds to the safety level, namely below 0.1–1.0 ppm (Naknikham et al., 2019).

Since phenols and phenolic compounds are chemically stable and highly soluble in water, phenols abatement is a challenge for the traditional wastewater treatment plants (Ganguly et al., 2020). In addition, advance tertiary wastewater treatment technologies are still costly and often require consumption of additional chemicals and energy.

The significance of the TiO₂-GO interface for substrates like phenol, which typically do not exhibit significant adsorption on GO—a common characteristic of most water micropollutants—has been discussed, with the photocatalytic activity being primarily influenced by the GO loading.

Graphene-titanium dioxide (GT) composites was prepared economically, with low-energy and low-chemical consumption, nearly neutral pH, and environmentally friendly syntheses. Materials were produced with a constant structure, even by using different types of reactors for the synthesis. The synergy between GO and TiO₂ appeared to depend on interface. Therefore, the materials with the highest phenol photodegradation activities were those with a 0.05 wt. % GO loading. Conversely, materials with GO loading higher than 0.5 wt. % exhibited lower activity compared to the pure TiO₂ (Naknikham et al., 2019).

Oxygen functional groups generated in graphitic sheets do not increase linearly with chemical oxidation time in graphite oxide; only some morphological changes are observed in terms of stacking and roughness with variation in this parameter (Bustos-Ramirez et al., 2015). However, in obtaining graphene oxide using an ultrasonic bath with degassing, modification of the other parameter produces changes in the graphene oxide sheets. This removes oxygenated functional groups and affects the photocatalytic activity of graphene oxide. On the other hand, the number of layers and their dimensionality are also a factor affecting photocatalytic activity in this case and led to a difference between the effectiveness of graphite oxide and graphene oxide. It is found that GEO-2-55 is the graphitic nanometric material that presents the best photocatalytic activity (Bustos-Ramirez et al., 2015). The combination of oxygenated functional groups, the band gap range (1.8-4 eV), and the roughness in the sheet are more efficient with the incidence of UV light at 254 nm than only photolysis or adsorption process.

The removal of 38% of the phenol in water with GEO-2-55 is a very favorable result and makes this material viable and efficient for applications in alternative advanced oxidation processes (Ramírez et al., 2017).

Hydroxy and other functional derivatives of benzoic acid are included in the term "phenolic acid." They play a vital role in controlling plant growth and disease resistance in addition to guaranteeing the formation of lignin. The development of certain diseases is linked to the involvement of proteins and growth regulators, as well as hydroxy-cinnamic acids. Moreover, their significance for chloroplasts and the photosynthesis process may also exist. It has been demonstrated that benzoic acid prevents photosynthesis in spinach chloroplasts. The most common plant phenolic compound is p-Coumaric acid (Kaurinovic & Vastag, 2019). In addition, Rosmarinic acid possesses antibacterial, anti-inflammatory, and antioxidant properties. Compared to vitamin E, it has a stronger antioxidant effect. Rosemary acid lowers the risk of atherosclerosis and cancer by preventing damage to cells caused by free radicals

(Nadeem et al., 2019). In contrast to antihistamines, rosemary acid inhibits the immune system cells that trigger swelling and fluid retention from activating. It is used to treat bronchial asthma, cancer, cataracts, arthritis, and stomach ulcers. Compared to other antioxidants, caffeinic acid significantly lowers the production of α -toxin by over 95%. Large doses of coffee acids have been shown to cause gastric papillomas in rats, which is detrimental to their health. On the other hand, when various antioxidants, such as baconic acid, were combined with these coffee acids, the same rats experienced a significant reduction in colon tumors. It is unknown if bicarbonate poses a health risk to humans (Salim et al., 2023).

When skin is exposed to ultraviolet radiation, particularly UVC and UVB rays, calcium acid and its derivative caffeic acid phenethyl ester (CAPE) reduce tumor growth and exhibit anti-inflammatory and anticancer properties (Ozturk et al., 2012). Mice whose skin was treated with bee propolis and a papilloma-causing agent (TPA) showed anticancer activity. There were substantially fewer papillomas as a result of CAPE (Forma & Brys, 2021). The primary classes of phenolic compounds are depicted in Figure 2.

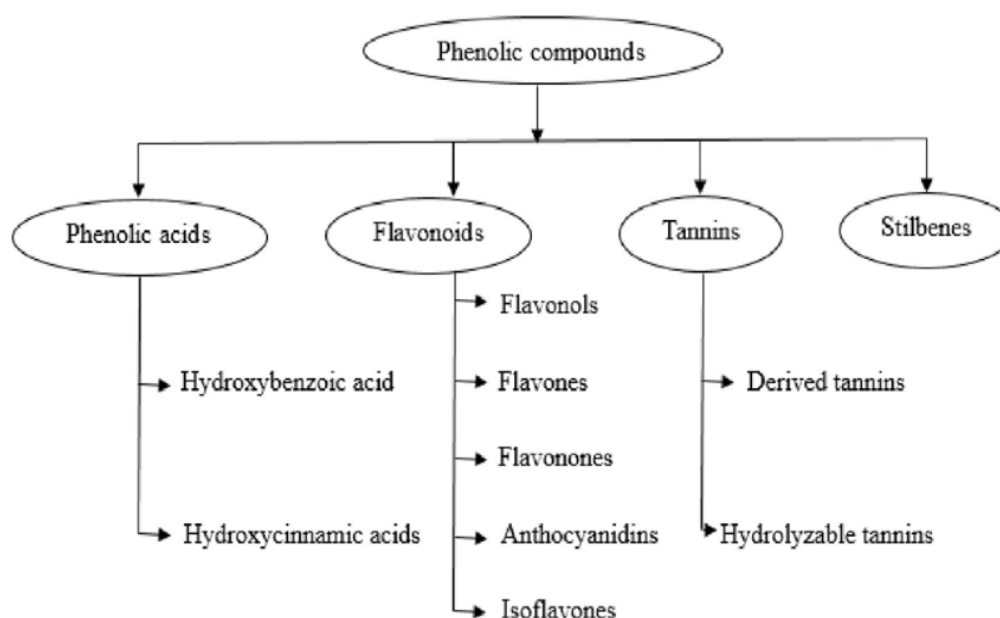


Figure 2: Principal groups of compounds containing phenols (Alara et al., 2021)

THE ROLE OF FLAVONOIDS IN THE SYNTHESIS OF GRAPHENE OXIDE

There is a great ecological significance to flavonoids. They serve as antimicrobial agents, signal molecules for beneficial microorganisms for the plant, and pigments that draw in insect pollinators. Yellow flavones and flavonols are particularly significant in this regard. Flavonoids shield plant tissue from UV radiation due to their strong absorption of UV light, which affects essential chloroplast functions (Rogowska-van der Molen et al., 2023). Flavonoids are secondary metabolites of plants that have a polyphenolic structure, just like phenolic acids. The polypropanoid pathway is used in their synthesis, with the phenylalanine molecule serving as the catalyst. These substances have different effects on biology. They are



divided into smaller groups (Figure 2). Additional common groups of flavonoids are condensed tannins, xanthonenes, and auronenes.

Though they are rarely found as their glycosides, leucoanthocyanidins and catechins share a similar structure. We encounter flavonoids in our daily lives for the most part. Many of the approximately 6000 flavonoid compounds that have been isolated and identified thus far are widespread in higher plants. The majority of flavonoid substances that frequently gather in plant cell vacuoles are glycosides (Ullah et al., 2020).

The range of pharmacological activities is generally attributed to secondary metabolites of a phenolic nature, such as flavonoids (Agidew, 2022). As hydroxylated phenolic compounds, flavonoids are known to be produced by plants in reaction to microbial infection (Roy et al., 2022). The majority of the antioxidant activity found in plants or plant-derived products is attributed to phenolics, the largest class of phytochemicals; flavonoids are the largest class of naturally occurring phenolic compounds, found in various plant parts both in their free form and as glycosides (Sulaiman & Balachandran, 2012). While there have been some reports of saponin involvement, numerous studies have emphasized the role of various phenolic and flavonoid compounds in the synthesis of nanoparticles (Kalu et al., 2022).

Calotropis procera, a variety of milk weed, is a well-known medicinal plant that grows widely throughout the world. Its phytochemicals have been linked to its reported anticancer, anticoagulant, antioxidant, anti-inflammatory, and antipyretic effects (Morsy et al., 2016).

It has been reported that zinc oxide (Abomuti et al., 2021), silver nanoparticles (Sadowski, 2010), cerium oxide nanoparticles (Shittu & Stephen, 2016), and gold nanoparticles can be synthesized using aqueous extracts of *Calotropis procera*. It is necessary to determine the phytochemicals present and their effects on significant magnetite properties because this plant is widely available and may be used to synthesize magnetites due to reports of their presence.

The method outlined by Dhar et al., (2021) was used to prepare the *Calotropis procera* aqueous extract. The phytochemicals, primarily phenols, flavonoids, alkaloids, tannins, glucosides, and saponins, were screened out of the aqueous *Calotropis procera* leaf extract. Using the Folin-Ciocalteu method as outlined by Amrulloh et al., (2021), the total phenol content of the leaf extract was ascertained. Using the aluminum chloride method as reported by Chang et al., (2020), the total flavonoid content of the aqueous leaf extract was ascertained. Ethanol extraction method was used to determine the total alkaloid, cardiac glucoside, and saponin of the aqueous leaf extract (Pandey & Sharma, 2022). Using the procedure outlined in AOAC (2015), the crude extract's tannin content was ascertained.

Table 3: Phytochemical Analysis of *Calotropis procera* Extract (Kalu et al., 2022).

Phytochemicals	Presence (+)/Absence (-)	Total Content
Cardiac glycoside	-	
Saponins	+	24.42 ± 1.96 (mg g ⁻¹)
Tannins	+	25.95 ± 1.94 (mg g ⁻¹)
Alkaloids	+	28.38 ± 1.78 (mg g ⁻¹)
Flavonoids	+	33.83 ± 2.18 (mg QE g ⁻¹)
Phenols	+	43.05 ± 2.25 (mg GAE/g)

The information was presented as the average of three duplicates standard deviation (±SD)



CONCLUSION

In conclusion, the synthesis and application of nano graphene oxide hold significant promise across various fields, with phenol and flavonoid playing pivotal roles in enhancing their properties and functionalities. Phenol enhances the photocatalytic activity of graphene oxide, particularly in the degradation of water micropollutants, while flavonoids act as effective reducing and stabilizing agents during synthesis, leading to the production of high-quality nano graphene oxide materials. The synergistic effects of phenol and flavonoid offer opportunities for the development of advanced graphene oxide-based materials with enhanced properties, applicable in diverse fields such as environmental remediation, energy storage, and biomedical engineering.

Moreover, the beneficial effects of phenolics on human health, as evidenced by improved health outcomes and reduced disease risks associated with the consumption of cereals, vegetables, and fruits rich in phenolic compounds, underscore the importance of understanding their role in nano graphene oxide synthesis and application. Researchers have actively pursued techniques for the extraction, separation, and quantification of phenolics from natural sources, with a focus on developing methods that are simple, rapid, environmentally friendly, and comprehensive. This review has provided insights into the significance of phenol and flavonoid in the synthesis and application of nano composites derived from plant-based sources, alongside advancements in separation and identification methods for plant phenolics. Continued research efforts in this area are vital for fully elucidating the mechanisms underlying the interactions between phenol, flavonoid, and nano graphene oxide, thereby facilitating the design and optimization of novel nanostructured materials with tailored functionalities and improved performance.

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