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Exploring Type-II Diabetes Potential of Phyto-Derived Carbon Dots

Lovish Sharma[1,*], Ankur Thakur[1], Komal Pathania[1]

Abstract

The integration of phytoconstituents with carbon dots (C-dots) presents a novel and sustainable approach to the development of nanotherapeutics for type 2 diabetes mellitus (T2DM). C-dots, zero-dimensional carbon-based nanomaterials, exhibit unique physicochemical properties including high fluorescence, tunable surface chemistry, biocompatibility, and low toxicity. Their ability to enhance the solubility, bioavailability, and targeted delivery of poorly soluble phytochemicals renders them highly suitable for biomedical applications. This study explores the synthesis of C-dots from phyto-derived waste materials via top-down and bottom-up approaches, including hydrothermal, microwave-assisted, and thermal decomposition methods. It further examines the methodologies for phytoconstituent loading – such as in-situ incorporation, post-synthesis adsorption, chemical conjugation, and encapsulation – highlighting their influence on therapeutic efficacy and release profiles. Functionalization with bioactive plant-derived compounds (e.g., curcumin, berberine, quercetin) enhances the anti-diabetic potential of C-dots by modulating oxidative stress, improving insulin sensitivity, and regulating glycemic indices. Recent advancements, including zinc-doped and enzyme-functionalized C-dots, have demonstrated enhanced wound healing and oral insulin delivery, expanding their utility beyond glycemic control. The theranostic capabilities of these nanostructures enable simultaneous diagnosis and treatment, positioning phytoconstituent-loaded C-dots as a versatile platform in diabetes management. Despite promising preclinical evidence, challenges such as reproducibility, pharmacokinetic profiling, and regulatory approval persist. This review underscores the need for standardized synthesis protocols and comprehensive in vivo validation to facilitate clinical translation. Ultimately, phytoconstituent-loaded C-dots offer a green, cost-effective, and efficacious alternative to conventional anti-diabetic therapies with reduced systemic toxicity.

Keywords: Diabetes, carbon-dots, phytochemicals, nanotechnology, formulation

INTRODUCTION

The natural product represents a significant source of medicine and is recognized as a drug in various pharmacopeias, yet the processes of isolation and extraction remain challenging. Approximately half of the drugs available on the market originate from natural products, particularly those derived from plants. A new category has emerged, known as semisynthetic, semi-purified phytoconstituents, which encompasses a wide array of therapeutic applications and allows for extensive variations in chemical structures through minor modifications. The intriguing aspect of phytoconstituents is that much of the investigation focuses on crude extracts or fractions rather than on individual isolated compounds. This strategy effectively addresses multiple tasks, like the multi-targeting effect. At times, this action has been implemented solely because the principal compounds have not been identified. The delivery of phytoconstituents is an evolving field, driven by advancements in

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phytochemical and phytopharmaceutical sciences. Additionally, various economic, political, social, and cultural factors may contribute to the growing acceptance of natural products as medicinal alternatives. The delivery of plant constituents presents significant challenges and limitations, particularly concerning immunological responses, uptake efficiency at target tissues, high scaling costs, and unresolved environmental factors. In the development of the first line choice, the delivery of therapeutic molecules presents several challenges. Constituents are facing issues such as poor aqueous solubility, inadequate permeability at the biological site, short circulation time in biological fluids, and significant first-pass metabolism by the liver. The various problems associated with phytoconstituents require solutions through both classical and novel approaches, as illustrated in Figure 1.

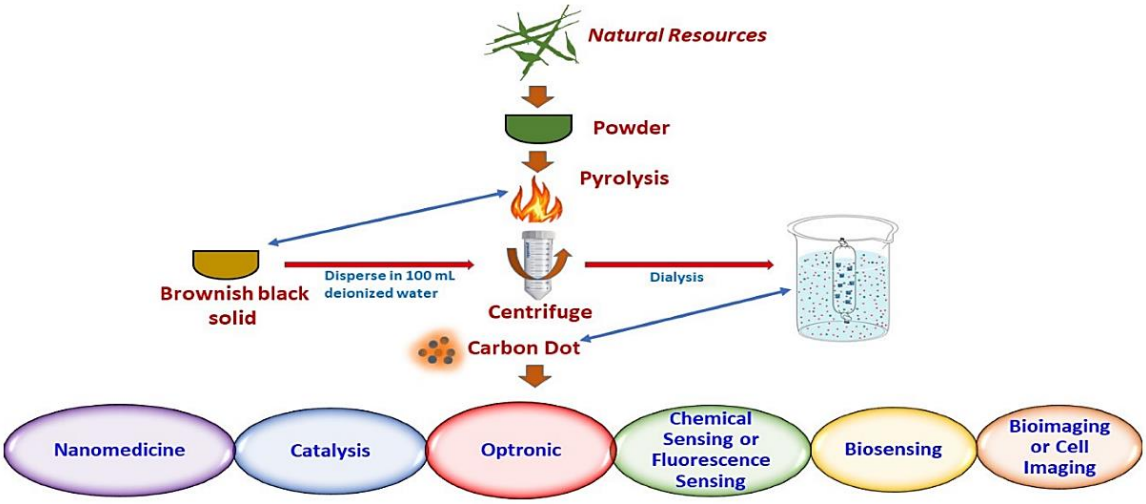

Figure 1. Carbon dot production from natural resources for various applications.

NANOTECHNOLOGY AS A SOLUTION FOR THE DELIVERY OF PHYTOCONSTITUENTS

The conventional delivery methodology for phytoconstituents faces numerous challenges, including issues related to aqueous solubility, instability, and permeability. Issues related to plant constituents can be effectively addressed through a nanotechnological approach, leading to enhanced safety, improved efficacy, and greater patient compliance. The active phytoconstituents are found in different parts of medicinal plants. Nanotechnology facilitates the development of nanomedicines and nanocarriers utilizing both pure active phytoconstituents and semi-purified extracts (Figure 2) [1–5].

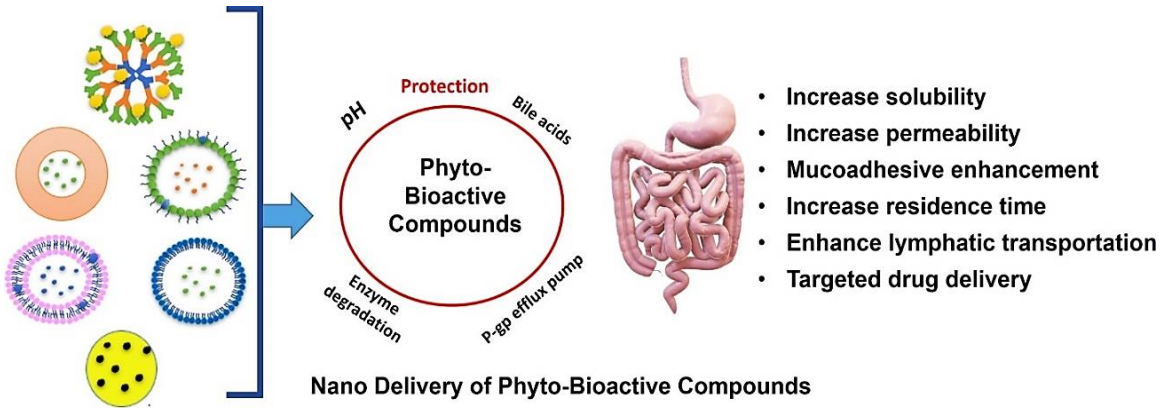

Figure 2. Nanotechnology as a solution for the delivery of phytoconstituents.

The application of nanotechnology significantly enhances outcomes by minimizing toxicity and adverse effects while generating greater therapeutic or pharmacological effects through the optimization of pharmacokinetic parameters. This accomplishment results from altering the surface chemistry and

properties, customized to meet specific requirements. The concept of nanotechnology has been explored to address challenges concerning activity, specificity, and bioavailability of phytoconstituents. The intricacies of phytochemicals can be effectively managed. The formulation at the nanoscale involves modifying release mechanisms, optimizing surface interactions, enhancing solubility, reducing loading units, minimizing degradation processes, and improving absorption and bioavailability. This figure illustrates the anticipated objectives of nano delivery carriers. The integration of nanotechnology with the delivery of phytoconstituents represents a significant advancement by improving effectiveness, selectivity, preventing degradation, and modifying release kinetics (Figure 2).

Diabetes

The disease can be categorized into two primary subclasses: insulin-dependent diabetes mellitus (type 1 diabetes) and insulin-independent diabetes mellitus (type 2 diabetes).

Type 1 DM is an autoimmune disorder characterized by the failure of insulin-producing pancreatic beta cells, leading to insulin deficiency that typically manifests at a young age. Conversely, type 2 diabetes mellitus involves a dual issue of cellular resistance to insulin along with inadequate insulin production, representing about 90% of individuals with diabetes [6, 7].

There is no clear evidence demonstrating a connection between type 1 DM and type 2 DM, even though both types exhibit numerous shared symptoms. DM causes impairment across all bodily systems, including the liver. Multiple mechanisms have been investigated to provoke liver injury in individuals with diabetes mellitus (Figure 3).

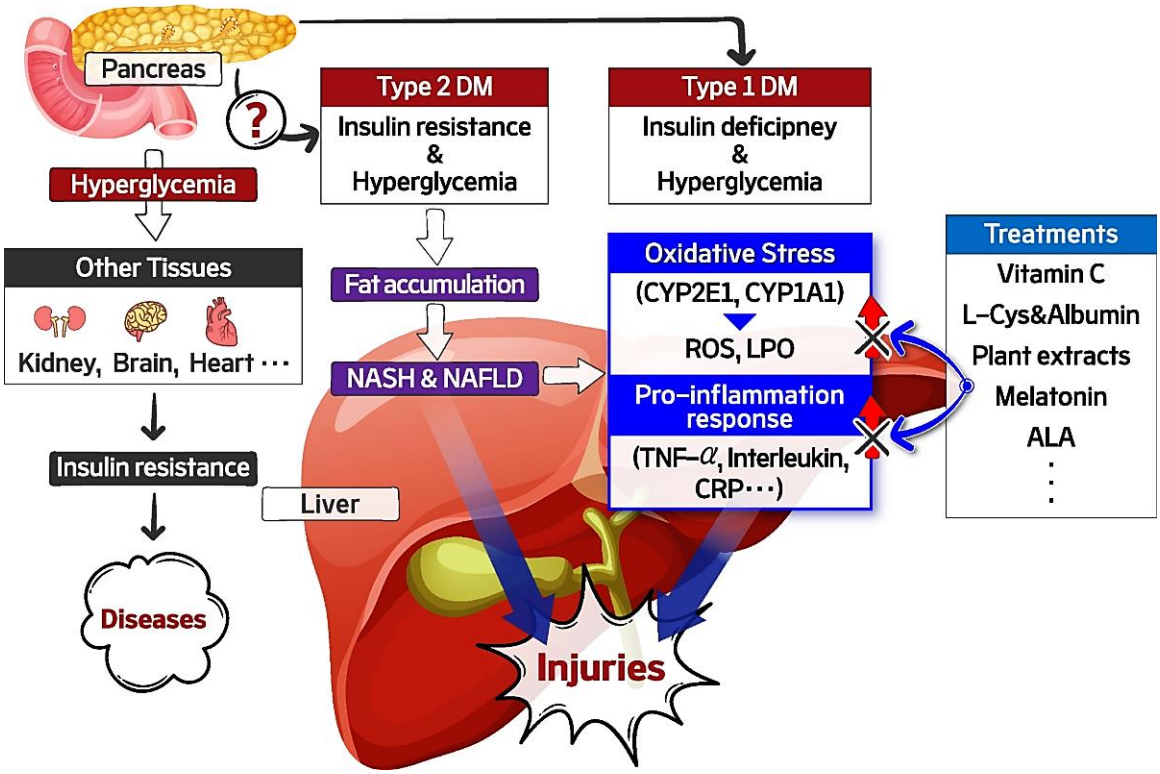

Figure 3. General understanding of diabetes.

These minuscule carbon structures, generally measuring between 1 and 10 nm, are part of a distinctive category of nanomaterials that exhibit a range of properties ideal for use in biomedical applications. Their attractiveness stems from the capability to meticulously manage their dimensions and surface chemistry, facilitating the customization of essential characteristics such as solubility, stability, and bioavailability. Furthermore, the surface modification of carbon dots (C-dots) allows for

customized interactions with biological entities, enhancing targeted drug delivery and optimizing cellular uptake. The intrinsic characteristics of quantum-sized C-dots position them as a highly promising platform for the advancement of sophisticated cancer therapeutics [8–12].

CARBON DOTS: SYNTHESIS & APPLICATIONS

C-dots are nanoparticles that are quasi-spherical and have a size of less than 10 nm, categorizing them as zero-dimensional entities. This material is regarded as an ideal carbon nanomaterial due to its remarkably high yield, low toxicity, excellent light stability, outstanding biological compatibility, and minimal synthesis cost. Carbon nanodots, including NCDs, CQDs, and GQDs, represent the standard classifications for C-dots. Altering the surface of carbon nanoparticles using polymeric and organic compounds is essential to produce C-dots. These zero-dimensional nanoparticles, generally measuring less than 10 nm, present significant potential for a variety of applications. C-dots are distinct, nearly spherical nanoparticles made up of sp2/sp3 hybridized carbon atoms. Additionally, carbon atoms facilitate the straightforward attachment of functional groups such as hydroxyl, carboxyl, and amine groups. Halogenation and cycloaddition represent significant chemical reactions employed to alter the surface characteristics of nanoparticles. Halogenation introduces halogens that can engage in further reactions with other groups, such as amines, leading to the formation of new functional structures. Meanwhile, cycloaddition facilitates the direct addition of a diverse array of functional groups. These modifications can customize the properties of nanoparticles for targeted applications across various domains such as medicine, electronics, and materials science.

Additionally, carbon atoms facilitate the straightforward attachment of functional groups such as hydroxyl, carboxyl, and amine groups. Halogenation and cycloaddition serve as chemical reactions that facilitate the modification of nanoparticle surfaces. Halogenation introduces halogens that can subsequently react with other groups, such as amines, to create new functional structures. In contrast, cycloaddition facilitates the direct addition of various functional groups. These modifications can customize the properties of nanoparticles for targeted applications across various domains such as medicine, electronics, and materials science.

In the synthesis of C-dots, diverse waste materials serve as carbon sources. Examples include orange peels and tea stems, along with other environmentally friendly options such as paper waste, plant extracts, fruit juice, residual tea waste, and various food sources from both animal and plant origins, including honey, meat, butter, and seafood. This reduces environmental pollution and improves economic advantages (Figures 4 and 5).

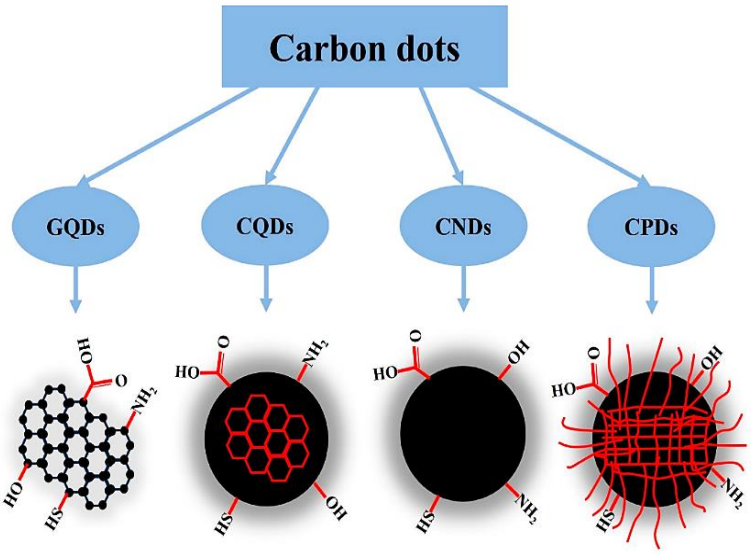

Figure 4. Types of carbon dots.

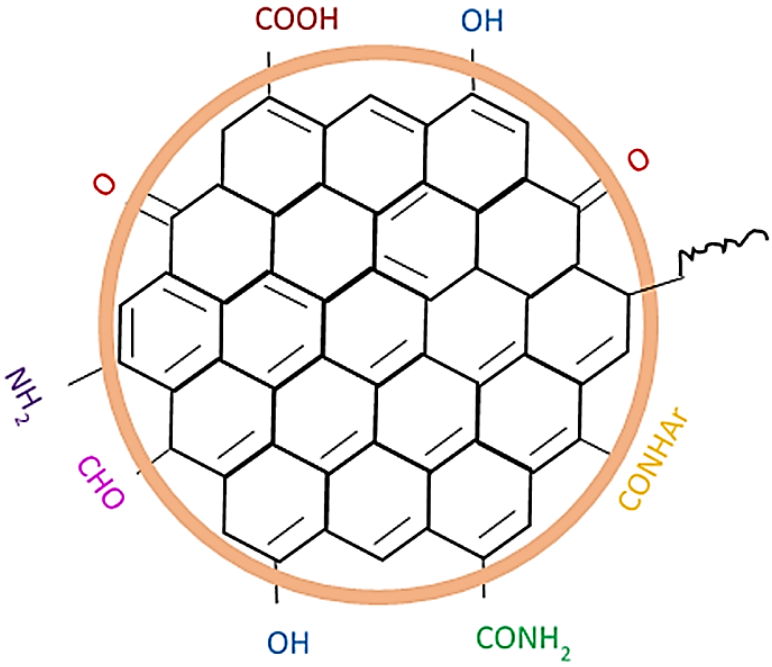

Figure 5. Structure of carbon dots.

The three focus areas of C-dots investigation include metal ion adsorption, fluorescence detection, and wound healing. Additionally, studies have demonstrated that C-dots exhibit numerous antibacterial properties, with their mechanisms of action including oxidative stress, physical damage, and inhibition of bacterial metabolic processes. The incorporation of C-dots, derived from sustainable sources, can enhance food packaging by prolonging shelf life and preserving the quality and freshness of food products. C-dots can be readily produced from waste or eco-friendly materials, such as fruits, peels, and leaves, as illustrated in Figure 6. The incorporation of active materials in food packaging enhances packaging functionality while also delivering economic advantages and promoting sustainability by minimizing environmental impact through effective food preservation and waste reduction (Figure 6).

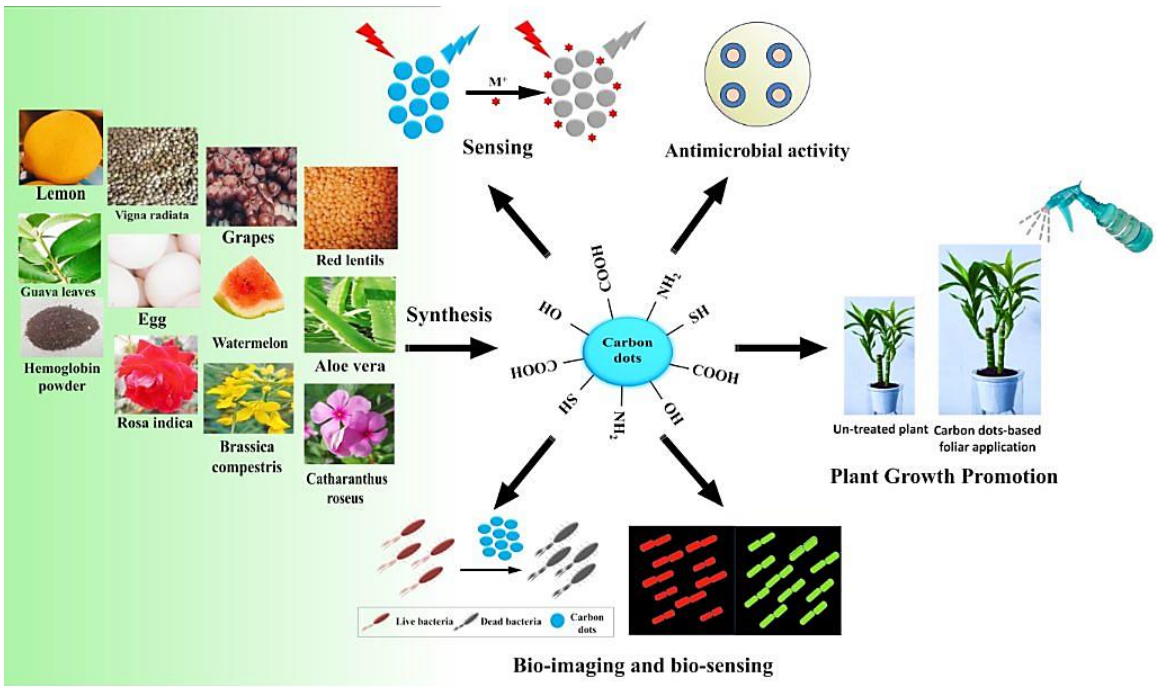

Figure 6. Environmentally friendly sources employed for the synthesis of C-dots and their applications.

Synthesis Methods

In the process of producing C-dots, various functional groups can be incorporated, such as hydroxyl, carboxyl, carbonyl, amine, and epoxy, among others. Furthermore, the incorporation of heteroatoms into C-dots through a range of biological, polymeric, and organic materials facilitates straightforward surface functionalization. Advancing our understanding, the characteristics of C-dots can be manipulated by modifying physicochemical properties using different precursors or alternative synthesis techniques. To attain notable surface characteristics for solvency and their beneficial applications, modifications to C-dots are essential. The synthesis of carbon dots encompasses a range of methods, each characterized by distinct variations and approaches. Presented below are several widely utilized methods for the synthesis of C-dots (Figure 7).

Figure 7. Synthesis methods to prepare carbon dots.

Top-Down Method

Currently, it is a prevalent approach to employ top-down techniques, such as electrochemical processes, laser ablation, arc discharge, and ultrasonic treatment, for the synthesis of C-dots from bulk carbon-based materials. Nonetheless, these methods are typically applied in environments characterized by elevated energy, significant potential, and high acidity. The top-down methods present significant challenges due to the severe conditions, in contrast to bottom-up processes [13].

Bottom-Up Approach

Due to their numerous advantages, such as a simple and convenient method, cost efficiency, accurate control, straightforward instrumentation, encouraging practical use, and bottom-up approaches, are presently trending.

Thermal Method

A highly effective method for synthesizing C-dots is through thermal breakdown, which involves the pyrolysis or carbonization of larger carbonaceous precursors at elevated temperatures. This method offers numerous benefits, such as the ability to produce C-dots in large amounts, cost-effectiveness, reduced reaction times, enhanced precursor tolerance, solvent-free processes, and straightforward synthesis. Additionally, the thermal method has the potential to enhance the luminous characteristics of C-dots through the adjustment of reaction conditions [14].

Microwave-Assisted Method

Microwaves encompass a broad spectrum of electromagnetic waves ranging from 1 mm to 1 m. The microwave-assisted approach generates a homogenous temperature for the even dispersal of C-dots and is simple, inexpensive, quick, and requires shorter reaction times.

Hydrothermal Method

This approach to synthesizing C-dots is cost-effective, safe for the environment, and non-toxic. This process involves the encapsulation of organic solvents as precursors, followed by their reaction under elevated pressures and temperatures within a hydrothermal reactor. The hydrothermal carbonization (HTC) process can generate C-dots from diverse raw materials such as proteins, chitosan, citric acid, glucose, and others.

Applications of Carbon Dots

C-dots have surfaced as exceptionally functional nanomaterials, characterized by their photoluminescence, biocompatibility, environmental friendliness, and surface tunability. C-dots present a compelling platform for a variety of applications in biological, environmental, and energy sectors. Their multifunctional properties, combined with outstanding biocompatibility and environmental friendliness, make them suitable for bioimaging, biosensing, medical diagnosis, catalysis, multicolour light-emitting diode production, phototherapy, drug and gene delivery, food safety, and energy conversion (Figure 8). Their applications extend into various domains.

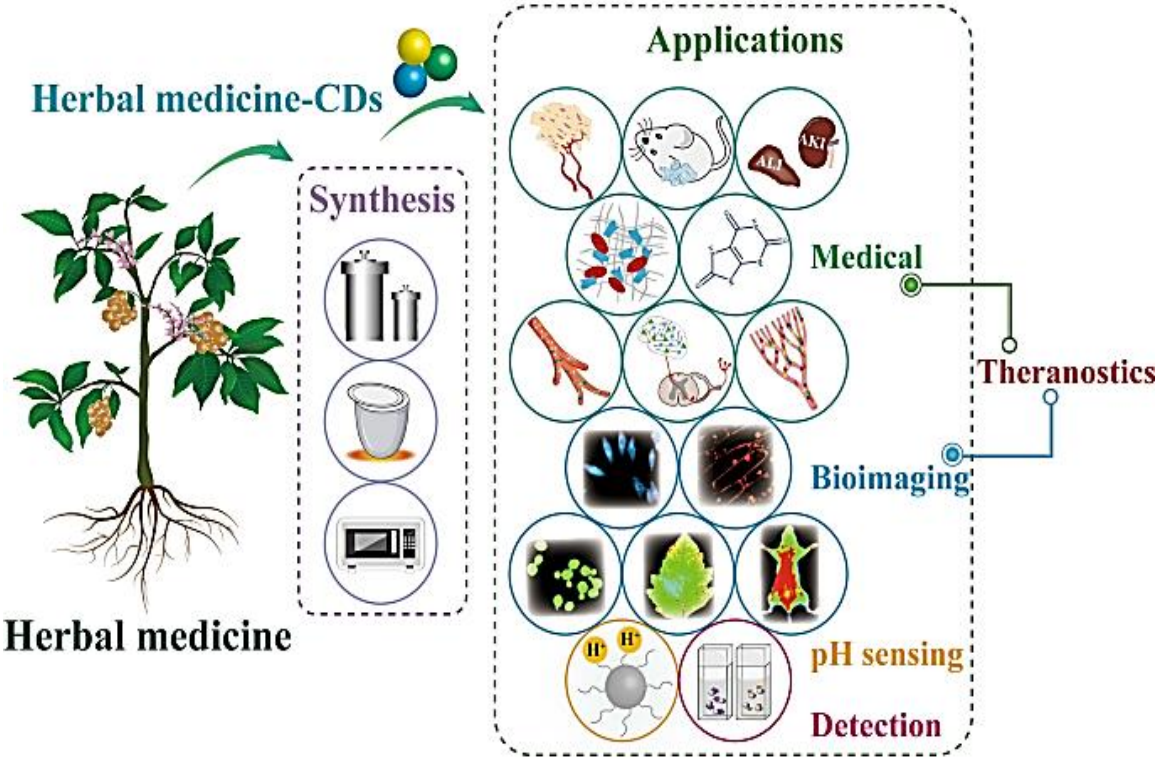

Figure 8. Herbal medicine-derived carbon dots.

Bioimaging

C-dots serve as efficient fluorescent probes for cellular and in vivo imaging due to their bright and tunable emission, photostability, and low cytotoxicity, making them suitable alternatives to traditional quantum dots.

Biosensing

Their fluorescence is sensitive to analytes, enabling C-dots to detect metal ions, biomolecules, and pathogens. They are widely applied in FRET and turn-off/turn-on sensors.

Medical Diagnostics

C-dots, when conjugated with targeting ligands, enable precise imaging and early diagnosis of diseases, including cancer, due to selective accumulation in diseased tissues.

Phototherapy

They act as photosensitizers in photodynamic therapy (PDT) and photothermal agents in photothermal therapy (PTT), generating ROS or heat under light to destroy cancer cells.

Drug and Gene Delivery

Owing to their functionalizable surface, C-dots can carry drugs, DNA, or RNA, releasing them in a stimuli-responsive manner for targeted therapeutic action.

Catalysis

C-dots catalyze redox reactions and degrade pollutants under light, making them valuable in photocatalysis and electrocatalysis, especially in water splitting and pollution remediation.

LEDs and Optoelectronics

They are used in multicolored and white light-emitting diodes due to their strong, tunable luminescence, solution processability, and eco-friendly synthesis.

Food Safety

C-dots detect food contaminants such as pesticides, toxins, and pathogens via fluorescence sensing, contributing to rapid quality assurance.

Energy Conversion and Storage

Integrated into solar cells and supercapacitors, C-dots enhance light absorption, charge transfer, and stability, improving energy device performance.

Environmental Monitoring

They detect pollutants (e.g., heavy metals, phenols) and degrade organic contaminants through photocatalysis, promoting green environmental solutions (Figure 9).

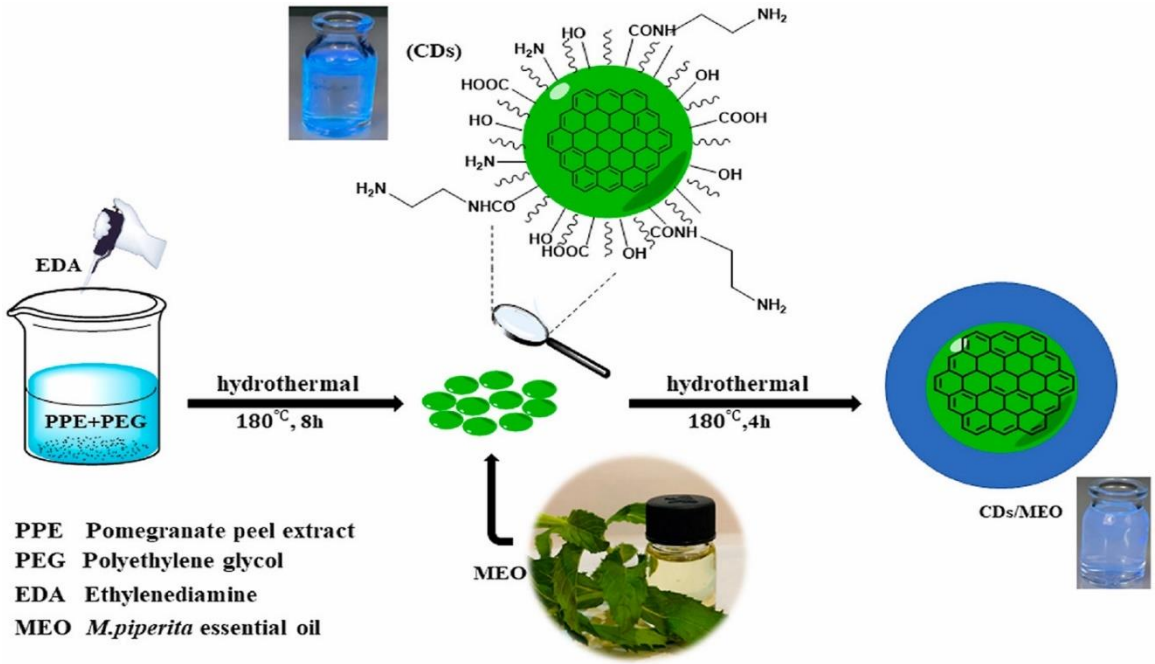

Figure 9. Phytochemicals loaded in C-dots.

PHYTOCHEMICAL LOADED IN CARBON DOTS

Phytoconstituent-loaded C-dots have surfaced as a noteworthy advancement in medicine, presenting diverse applications in disease diagnosis, drug delivery, and therapy. C-dots are a distinctive category

of fluorescent carbon-based nanomaterials that have attracted considerable interest because of their remarkable optical characteristics, compatibility with biological systems, minimal toxicity, and ease of surface modification. The incorporation of bioactive plant-derived molecules, often known as phytoconstituents, into these nanomaterials leads to synergistic effects, enhancing their suitability for biomedical applications. The integration of green nanotechnology and phytochemistry has resulted in the creation of phytoconstituent-loaded C-dots, providing safe, sustainable, and multifunctional platforms for disease diagnosis, drug delivery, and therapeutic interventions (Figure 9).

Methods of Loading Phytoconstituents into Carbon Dots

The incorporation of phytoconstituents into carbon dots represents a crucial advancement in the development of efficient nanotherapeutic and diagnostic agents. The loading method influences not only the efficiency of drug delivery and bioactivity but also determines the physicochemical properties, stability, and release profile of the final nanocomposite. The integration of phytochemicals into carbon dots can generally be accomplished through two primary methods: in situ loading and post-synthesis loading. Each method entails distinct strategies, tailored to the characteristics of the phytoconstituents and the desired biomedical application.

In-Situ Loading (One-Pot Synthesis Method)

In this approach, phytoconstituents are introduced during the synthesis of carbon dots. The phytochemical acts either as:

- a carbon precursor (main substrate), or
- a co-reactant (along with other precursors such as citric acid, PEG, or EDA).

Mechanism

During hydrothermal, solvothermal, or microwave-assisted carbonization processes, the phytoconstituents are integrated into the carbon framework. This results in a homogeneous distribution of bioactive molecules either embedded within or functionalized onto the surface of the C-dots.

Post-Synthesis Loading (Surface Adsorption or Conjugation)

In this method, C-dots are first synthesized using standard carbon sources. Phytoconstituents are then loaded onto the preformed C-dots using one of the following strategies:

Physical Adsorption

- Based on non-covalent interactions such as hydrogen bonding, π–π stacking, van der Waals forces, or electrostatic attraction.
- Simple mixing or sonication of C-dots with the phytochemical solution leads to spontaneous adsorption.

Chemical Conjugation

- Covalent bonding of phytoconstituents to functional groups on the C-dot surface using linkers such as EDC/NHS (for carboxyl-amine coupling).
- Offers more stable and controlled release profiles.

Encapsulation or Entrapment

- Phytochemicals are trapped within a polymeric or lipid coating formed over the C-dots.
- Used for unstable or hydrophobic plant compounds that require protection from degradation.

Solvent Evaporation and Emulsion Techniques

These techniques are occasionally employed when phytoconstituents are hydrophobic or volatile. The process involves:

- Dissolving phytochemicals and C-dots in suitable solvents,
- Creating an emulsion (e.g., oil-in-water),

- Evaporating the solvent under reduced pressure to form nanocomposites.

Such methods are particularly useful in food-grade or cosmetic formulations of phytochemical-loaded nanodots.

pH-Induced or Temperature-Induced Loading

This approach takes advantage of the pH- or temperature-responsive behavior of certain phytoconstituents and functionalized C-dots. Loading is carried out under specific conditions (e.g., acidic pH or mild heat), followed by stabilization.

CARBON DOTS IN DIABETES TREATMENT

The integration of phytoconstituents with carbon dots (CDs) has emerged as a promising strategy in the development of anti-diabetic therapies. Phytoconstituents, bioactive compounds derived from plants, have shown potential in managing diabetes due to their anti-diabetic properties. However, their clinical application is often limited by poor solubility, stability, and bioavailability. Carbon dots, small carbon-based nanoparticles, have gained attention for their ability to enhance drug delivery, improve bioavailability, and provide targeted therapeutic effects (Figures 10–12).

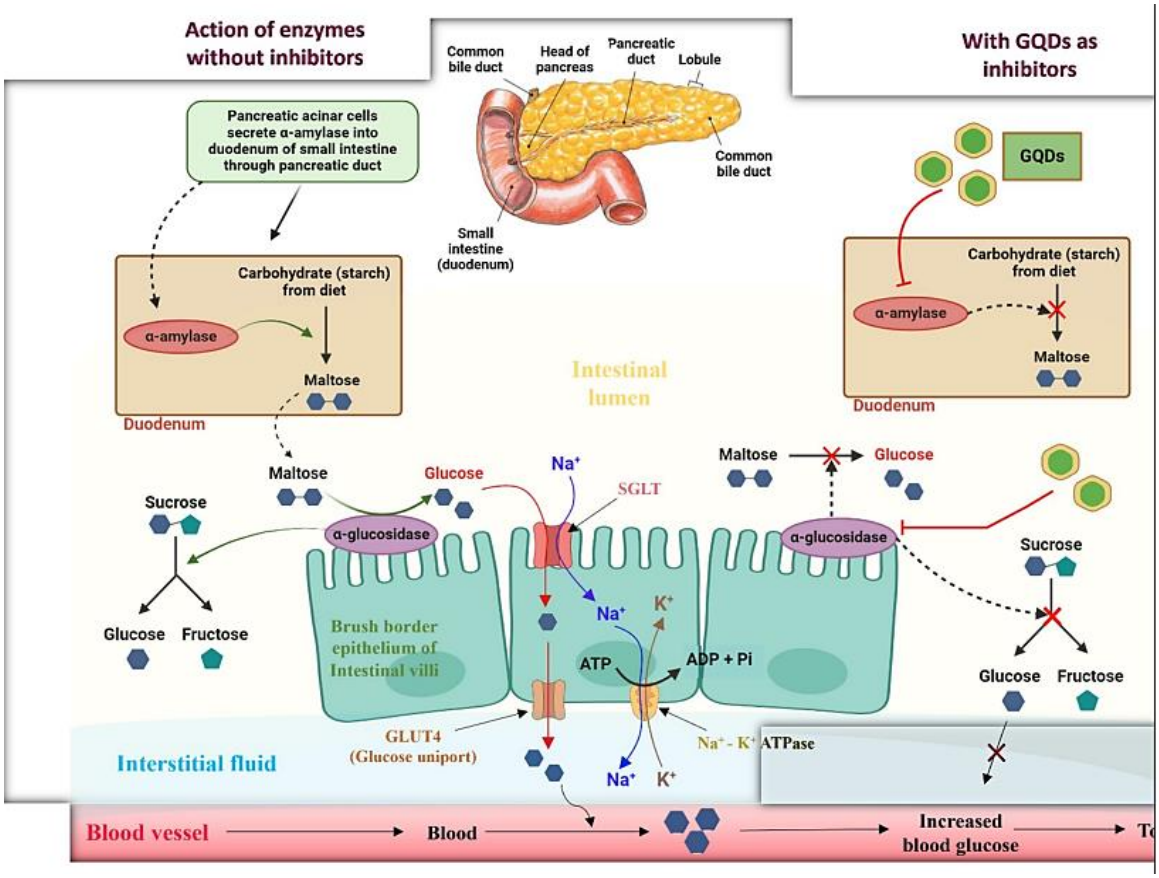

Figure 10. Hypothetical mechanism of GQDs for anti-diabetic activity.

Rationally developed and synthesized ultra-small carbon dots (C-dots) loaded with zinc single-atom nanozyme (Zn/C-dots) with the aim of promoting wound healing by nanocatalytic treatment, especially targeting its complex pathological microenvironment (Dai et al., 2024). Zinc single atoms and C-dots form a dual catalytic system with higher enzymatic activity. Zinc can synergistically increase the antibacterial action of C-dots (the effective antibacterial rate of 100 μg/mL Zn/C-dots was above 90 %). Unlike traditional C-dots, Zn/C-dots can cause endothelial cell migration and the formation of new blood vessels.

This study, by Camlik et al., 2022, aimed to examine whether carbon quantum dots can be used to transport insulin through the oral route and whether they can protect insulin from gastrointestinal enzymes, as they can easily pass through both cell membranes and biological walls. It is also aimed to reveal the mechanism by which this effect occurs.

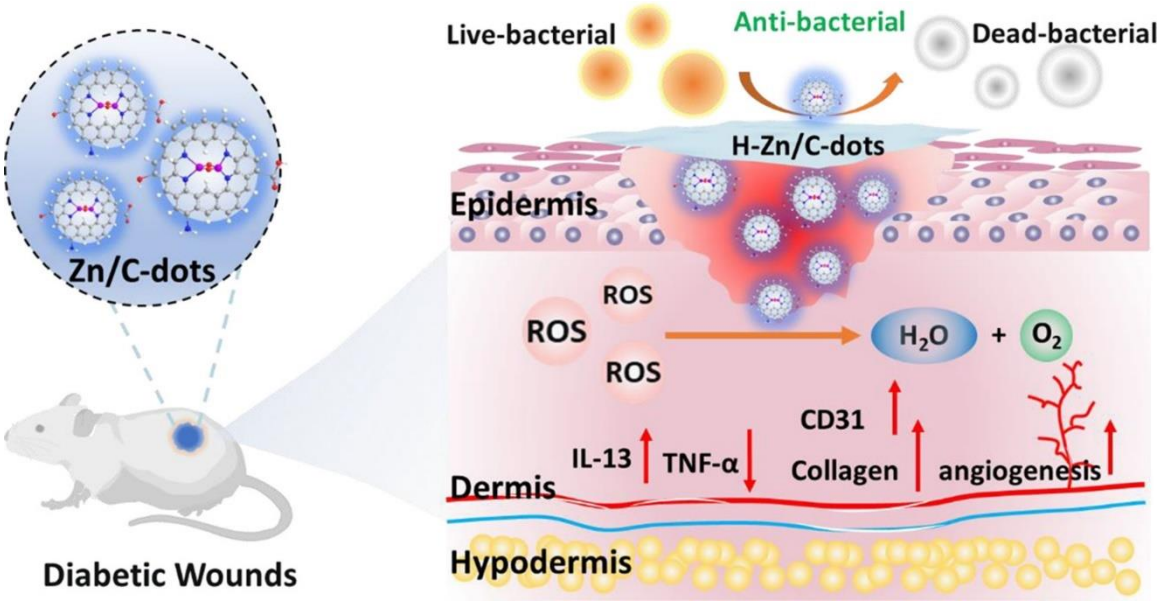

Figure 11. Ultra-small carbon dot with a zinc single-atom nanozyme.

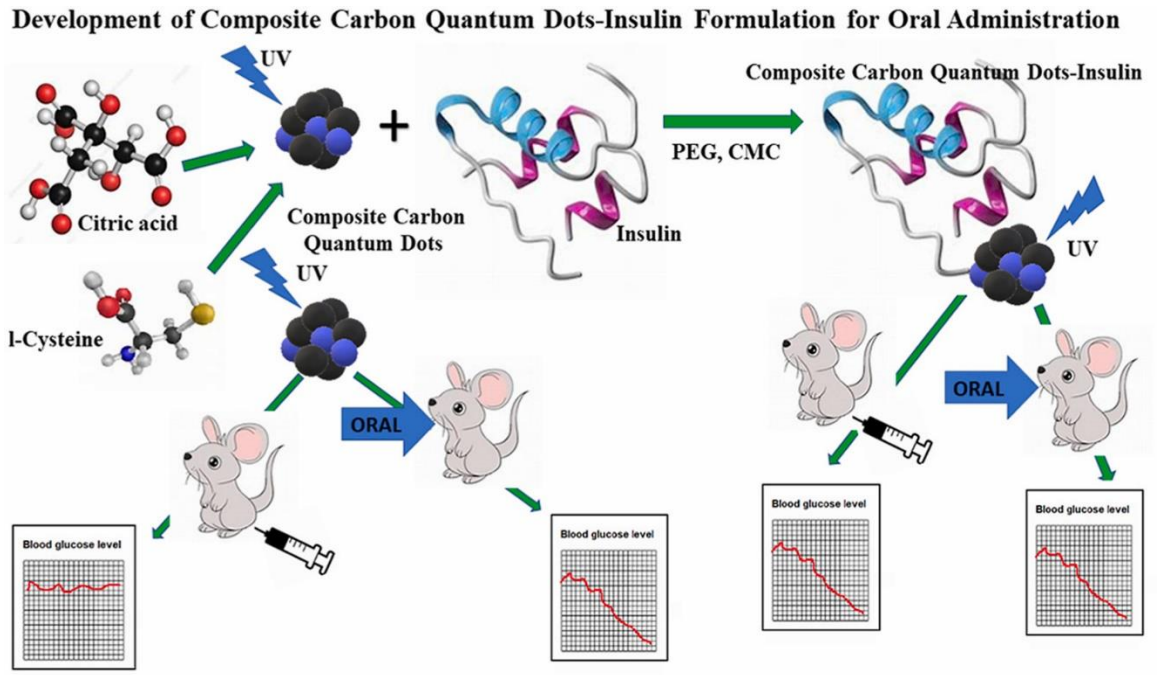

Figure 12. Carbon quantum dots-insulin formulation for oral administration.

CONTEXT OF THE STUDY

Diabetes management with conventional allopathic medications, such as sulfonylureas, metformin, and insulin analogs, is effective but often associated with significant toxicity and side effects, including:

- Hepatotoxicity (liver damage).
- Nephrotoxicity (kidney strain).
- Hypoglycemic episodes.

- Weight gain and gastrointestinal issues.

These risks are amplified with long-term use, and many patients develop tolerance or dependence on higher doses over time.

This study is important because it proposes a low-toxicity, high-efficacy alternative to conventional drugs by integrating phyto-constituents with carbon dot nanotechnology, addressing both the therapeutic and safety challenges in current diabetes management (Tables 1 and 2).

Table 1. Literature review.

S.N.	Author, Year, Journal	Title	Key Findings	Research Gap Addressed
1	Biology (Tran et al., 2020) [14]	Drug DiscBioactive Compounds in Anti-Diabetic Plants: From Herbal Medicine to Modern Drug Discovery	Pharmacological effects of plant-derived bioactive compounds with antidiabetic efficacy surpassing conventional drugs. Emphasizes pharmaceutical industry interest in phytochemicals.	Lack of mechanistic studies on bioactive compounds and clinical trials comparing efficacy/safety with modern drugs. No analysis of interactions between plant compounds and conventional medications.
2	Critical Reviews in Food Science and Nutrition (Zhao et al., 2019) [15]	Regulation of glucose metabolism by bioactive phytochemicals for the management of type 2 diabetes mellitus.	Bioactive phytochemicals improve insulin sensitivity and glucose uptake. Gut microbiota interactions with phytochemicals may aid T2DM management.	Need for early-stage T2DM treatments. Limited understanding of the gut microbiota's role in insulin resistance and glucose metabolism.
3	Diabetes-metabolism Research and Reviews (Liang Zhi et al., 2008) [16]	Nanomedicine and its potential in diabetes research and practice	Nanomedicine innovations include non-invasive glucose monitoring and "artificial nanopancreas." Nano-encapsulation improves insulin delivery.	Nanoparticle toxicity concerns. Islet encapsulation faces challenges like hypoxic cell death and poor biocompatibility.
4	Journal of Herbal Medicine (Kazhila et al., 2019) [17]	Diabetes mellitus and nature's pharmacy of putative antidiabetic plants	Identifies plants with antidiabetic properties but highlights variability in study methodologies.	Lack of standardized clinical trials and a mechanistic understanding of plant-derived compounds.
5	Current Diabetes Reviews (Munhoz et al., 2017) [18]	Isolated Compounds from Natural Products with Potential Antidiabetic Activity – A Systematic Review.	Identified compounds (e.g., quercetin, mangiferin) with antidiabetic mechanisms via in vitro assays.	Insufficient in vivo studies to validate findings. Limited evidence on the therapeutic use of plant species.
6	Journal of Nanobiotechnology (Kang Luo et al., 2021) [19]	Herbal medicine-derived carbon dots: synthesis and applications in therapeutics, bioimaging, and sensing.	Herbal-derived carbon dots (HM-CDs) show promise in diagnostics and therapeutics. Microwave synthesis is recommended for stability.	HM-CDs' components and synthesis methods need optimization. Lack of understanding of therapeutic mechanisms.
7	Molecules (Mayadah et al., 2021) [20]	Plants' Secondary Metabolites as Blood Glucose-Lowering Molecules	Secondary metabolites (e.g., flavonoids, alkaloids) improve insulin signaling and inhibit carbohydrate digestion.	No specific gaps mentioned. Future research is needed on long-term effects, dosages, and drug interactions.

8	Pharmacological Research (Ungurianu et al., 2019) [21]	Preclinical and clinical results regarding the effects of a plant-based antidiabetic formulation versus well-established antidiabetic molecules.	Plant-based formulation (PBAF) improves HDL/LDL functionality and redox status. Metformin outperforms in reducing glycation.	Limited molecular mechanism studies. Need for prospective clinical trials on PBAF's long-term safety.
9	Antioxidants (Shanmugapriya et al., 2023) [22]	Antioxidant Phytochemicals as Potential Therapy for Diabetic Complications	Polyphenols reduce oxidative stress and inflammation via SIRTs and Nrf2 pathways.	Need to study polyphenols' effects on coenzyme Q and ferroptosis. Limited therapies for diabetic nephropathy progression.
10	Current Pharmaceutical Biotechnology (Jeevanandam et al., 2015) [23]	Opportunities for Nano-Formulations in Type 2 Diabetes Mellitus Treatments.	Nanoparticles target cellular mechanisms to reverse insulin resistance.	Lack of detailed mechanisms for nanomedicine supplements. Unexplored opportunities in nano-formulations.
11	Current Diabetes Reviews (Nooreen et al., 2020) [24]	A Systematic Review on Synthetic Drugs and Phytopharmaceuticals Used to Manage Diabetes.	Herbal/nutraceutical therapies offer holistic diabetes management with fewer side effects.	Limited studies on synthetic-herbal drug interactions and long-term safety.
12	Studies in natural products chemistry (Cabañez et al., 2023) [25]	Structure-related relationship: Plant-derived antidiabetic compounds	Structure-activity relationship (SAR) analysis aids in developing safer antidiabetic analogs.	Need for SAR studies to optimize phytocompounds and understand metabolic pathways.
13	The Pan African (Great et al., 2023) [26]	Antidiabetic Phytotherapy	Plants, like bitter melon and cinnamon, enhance insulin sensitivity. Lack of standardized dosing.	Insufficient clinical evidence. Variability in bioactive compounds across plant sources.
14	International journal of membrane science and technology (Kumar Bera et al., 2023) [27]	Nanomaterials Drug Delivery System in Herbal Formulation for Antidiabetic Activity: A Review	Nanoparticulate systems enhance the bioavailability and efficacy of herbal extracts.	Challenges in scaling production and ensuring consistency. Limited clinical safety data.
15	Current Diabetes Reviews (Bhadouria et al., 2024) [28]	An Insight into Naturally Occurring Phytoconstituents and Novel Approaches Towards the Treatment of Diabetes	Nanoformulations of phytomolecules offer improved therapeutic effects over synthetic drugs.	Need for long-term safety evaluations and individualized treatment approaches.
16	Advances in Laser Science-I (Nasution et al., 2024) [29]	Antidiabetic activities of Phyllanthus emblica: An updated review	Fruit extracts reduce blood glucose, HbA1c, and oxidative stress. No studies on other plant parts.	No clinical trials conducted. Limited to fruit extracts.
17	Role of Flavonoids in Chronic Metabolic Diseases: From Bench to Clinic (Kumar et al., 2024) [30]	Flavonoids and Nanotechnology in Insulin Resistance and Diabetic Complications	Flavonoids mitigate diabetic complications. Nanostructures enhance solubility and absorption.	Lack of mechanistic insights. No long-term safety data for nanocarriers.
18	International Journal of Pharmaceutical Professionals' research (Shukla et al., 2024) [31]	A Review on Some Potential Traditional Phytomedicines with Antidiabetic Properties	Historical use of plants in Ayurveda aligns with modern antidiabetic research.	No specific gaps mentioned. Need to address current research gaps in traditional phytomedicine.

19	Current Analytical Chemistry (Chandra Arya et al., 2024) [32]	A Systematic Study of Pyracantha crenulata Phytoconstituents for their Anti-Diabetic Activity Using Computational Techniques	Molecular docking shows high dock scores for phytoconstituents compared to conventional drugs.	No in vivo/clinical validation. Limited mechanistic and safety data.
20	Heliyon (Azeem et al., 2024) [33]	Phytochemical-Functionalized Iron Oxide Nanoparticles for Enhanced Antidiabetic and Antioxidant Activity: A Novel Approach to Targeted Therapy for Type 2 Diabetes	Fe2O3 nanoparticles show 65.26% α-amylase inhibition and antioxidant activity.	No toxicity or stability studies. Mechanisms of action are unclear.
21	Phytotherapy Research (Roy et al., 2024) [34]	Herbal Approaches to Diabetes Management: Pharmacological Mechanisms and Omics-Driven Discoveries	Herbal compounds (e.g., berberine, EGCG) improve insulin sensitivity and reduce oxidative stress.	Lack of large-scale clinical trials. Need for biomarker selection and safety profiling.
22	Journal of disease and global health (Ibrahim et al., 2024) [35]	Nanotechnology Therapy for Type 2 Diabetic Mellitus: Challenges and Future Perspectives	Nanotechnology improves drug delivery and glucose monitoring but faces safety and regulatory hurdles.	Safety concerns, immunological reactions, and regulatory barriers are unresolved.
23	International journal of advancement in life sciences research (Shanmugapriya et al., 2024) [36]	Anti-Diabetic and Free Radical Scavenging Activity of Phytochemicals from Caesalpinia bonducella	Seed extract inhibits α-amylase (0.25 mg/mL) and shows 92.04% DPPH scavenging.	No in vivo studies. Mechanisms of enzyme inhibition are unclear.
24	Current Diabetes Reviews (Bhadouria et al., 2024) [37]	Nanotechnology-based Herbal Drug Formulation in the Treatment of Diabetes Mellitus	Nanocarriers improve herbal drug delivery but face formulation challenges.	Need for optimized formulations and safety studies.
25	Nanotechnology (Verma et al., 2024) [38]	Nanomaterials for diabetes: diagnosis, detection, and delivery	Injectable nano-networks improve glucose management in diabetic mice. Silica nanocarriers show tunable properties.	Low drug bioavailability and patient compliance issues. Limited long-term efficacy data.
26	Current Diabetes Reviews (Kaushik et al., 2024) [39]	Herbal Nanoformulations for Diabetes: Mechanisms, Formulations, and Clinical Impact.	Nanoformulations enhance bioavailability and glycemic control with minimal side effects.	Need for optimized formulations and long-term safety studies.
27	Pharmaceuticals (Hanan et al.,2024) [40]	Oral Active Carbon Quantum Dots for Diabetes	Metformin carbon quantum dots (MetCQDs) improve drug bioavailability.	Not specified.
28	Regenerative Biomaterials (Dai et al., 2024) [41]	MOF-Encapsulated Copper-Doped Carbon Dots Nanozymes with Excellent Biological Activity Promote Diabetes Wound Healing	ZIF-Cu/C-dots reduce inflammation and promote wound healing in diabetic mice.	Burst release and immunological clearance issues. No long-term safety data.
29	BIO web of conferences (Astuti et al., 2024) [42, 43]	Nanoparticles-mediated delivery of herbal extract: Impact on inhibition of advanced glycation end-product (AGEs): A systematic review	Nanoparticles enhance herbal extract bioavailability and reduce AGEs.	No long-term safety data. Mechanisms of nanoparticle-herb interactions are unclear.

Table 2. List of phytoconstituents for anticancer activity.

S.N.	Phytoconstituent	Source Plant
1	Berberine	*Berberis aristata*
2	Curcumin	*Curcuma longa (Turmeric)*
3	Quercetin	*Allium cepa, Moringa oleifera, etc.*
4	Resveratrol	*Vitis vinifera (Grapes)*
5	Epigallocatechin gallate (EGCG)	*Camellia sinensis (Green tea)*
6	Genistein	*Glycine max (Soybean)*
7	Kaempferol	*Apium graveolens, Camellia sinensis*
8	Apigenin	*Parsley, Chamomile*
9	Aloin	*Aloe vera*
10	Ginsenosides	*Panax ginseng*
11	Silymarin	*Silybum marianum (Milk thistle)*
12	Chlorogenic acid	*Coffea spp., Artichoke*
13	Rutin	*Fagopyrum esculentum (Buckwheat)*
14	Baicalein	*Scutellaria baicalensis*
15	Caffeic acid	*Coffea spp., Thymus vulgaris*
16	Luteolin	*Celery, Peppers*
17	Mangiferin	*Mangifera indica (Mango leaves)*
18	Gymnemic acids	*Gymnema sylvestre*
19	Punicalagin	*Punica granatum (Pomegranate)*
20	Myricetin	*Myrica spp., Teas*

CONCLUSIONS

Phytoconstituent-loaded C-dots represent a sustainable, biocompatible, and multifunctional nanotechnology platform that holds considerable promise for targeted therapies in diabetes management. The nanostructures, created using environmentally friendly techniques, utilize the healing properties of bioactive compounds from plants and display distinctive physicochemical traits, including their ultra-small size and fluorescence that depends on excitation. The inherent luminescence of these C-dots enables real-time imaging and localization at both cellular and tissue levels, rendering them exceptionally appropriate for concurrent diagnostic and therapeutic – theranostic applications. In the realm of diabetes management, phytoconstituent-functionalized C-dots present a compelling alternative to traditional therapies, facilitating efficient delivery throughout the body while reducing systemic toxicity. Future studies will concentrate on the careful refinement of synthesis protocols to ensure consistent results and scalability, both of which are crucial for clinical application. The functionalized C-dots will be subjected to thorough assessment for cytotoxicity, bioimaging effectiveness, and anticancer properties through established in vitro and in vivo models.

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