European Cells and Materials Vol.58 2026 (pages 102–118) DOI: 10.22203/eCM.v058a09 ISSN 1473-2262

Review

Traditional Chinese Medicine-Derived Carbon Dots Nanozymes for Treating Inflammatory Bowel Disease: Current Challenges and Future Perspectives

Chenye Huang[1,2,§], Chenxi Xu[3,§], Manli Cui[2], Yifan Li[1,2], Zhan Zhang[4], Qian Li[2,*] and Mingxin Zhang[2,*]

[1]Second Clinical Medical College, Shaanxi University of Chinese Medicine, 712046 Xianyang, Shaanxi, China
[2]Department of Gastroenterology, The First Affiliated Hospital of Xi'an Medical University, 710077 Xi'an, Shaanxi, China
[3]School of Basic Medical Sciences, Xi'an Jiaotong University Health Science Center, 710061 Xi'an, Shaanxi, China
[4]Division of Cardiology, Department of Medicine, Emory University School of Medicine, Atlanta, GA 30322, USA
[§]These authors contributed equally.

Abstract

Inflammatory bowel disease (IBD) is a chronic gastrointestinal disorder with a complex pathogenesis and limited therapeutic options. Nanozymes, particularly carbon dots (CDs), offer a novel strategy for treating IBD owing to their enzyme-like catalytic activities and high biocompatibility. Traditional Chinese medicine (TCM) involves the use of rich sources of bioactive compounds with anti-inflammatory and antioxidant properties; however, the clinical application of these compounds is often hampered by their low solubility and bioavailability. This review explored the effects of TCM-derived CD nanozymes (TCM-CDs) on enhancing IBD therapy. The classification, green synthesis methods, and unique mechanisms of TCM-CDs, including reactive oxygen species scavenging, regulation of gut microbiota, and modulation of inflammatory signaling pathways, were summarized. Furthermore, the current limitations in material synthesis, biological uncertainty, and clinical translation challenges were discussed; an AI-driven framework was developed for future precision design and personalized IBD treatment. TCM-CDs represent promising nanoplatforms that synergize the multitarget therapeutic advantages of TCM with the catalytic versatility of nanozymes, offering new insights into next-generation IBD therapeutics.

Keywords: Carbon dot nanozymes, traditional Chinese medicine, inflammatory bowel disease.

***Address for correspondence**: Qian Li, Department of Gastroenterology, The First Affiliated Hospital of Xi'an Medical University, 710077 Xi'an, Shaanxi, China. E-mail: liqian1103@126.com; Mingxin Zhang, Department of Gastroenterology, The First Affiliated Hospital of Xi'an Medical University, 710077 Xi'an, Shaanxi, China. E-mail: zmx3115@xiyi.edu.cn.

Introduction

Inflammatory bowel disease (IBD), including Crohn's disease and ulcerative colitis (UC), is a chronic nonspecific intestinal inflammatory disorder. The incidence rate of IBD is high in young and middle-aged populations. IBD exhibit a protracted course and recurrent episodes, reducing patient quality of life and imposing a large burden on societal healthcare resources [1]. The etiology of IBD remains unclear; however, IBD likely results from interactions among environmental factors, genetic susceptibility, gut microbiota dysbiosis, and immune system abnormalities. Currently, no cure exists for IBD; clinical treatments primarily aim to control symptoms, alleviate inflammation, and induce and maintain remission [2]. IBD are accompanied by long-term risk factors such as malignancy and infection [3]. However, traditional treatments, including glucocorticoids, immunosuppressants, and biologics, are not completely effective and produce adverse side effects, necessitating the development of novel and effective therapeutic strategies [4].

Nanozymes are nanomaterials ranging from 1 to 100 nm in size that exhibit enzyme-like catalytic properties [5,6]. Among the numerous nanozymes, carbon dot (CD) nanozymes have received considerable attention from the academic community due to their structure and certain performance characteristics [7]. The unique structure of CDs leads to high enzyme-like catalytic activity, ensures high biocompatibility, and enables their optical properties to be tuned [8,9]. CDs can mimic the catalytically active centers of various natural enzymes, demonstrating high enzyme-like activity and catalyzing substrates under physiological conditions [10–12]. CDs possess various enzyme-

like activities, such as those of peroxidase (POD), oxidase (OXD), superoxide dismutase (SOD), and catalase (CAT) [13]. POD, OXD, and SOD play crucial roles in regulating intracellular reactive oxygen species (ROS) homeostasis and catalyzing the generation of ROS, which are used in antibacterial and anticancer therapies. SOD and CAT are responsible for decomposing and scavenging ROS, which are thus suitable for anti-inflammatory and antioxidant treatments (Fig. 1). In addition to their enzyme-like activity, nanomaterials offer multiple other functions through various modifications such as alterations in size, shape, and surface properties [14].

The convergence of developments in nanotechnology and biomedicine has enabled progress in the research on the application of CDs in disease diagnosis and treatment. CDs particularly show potential for using in biosensing, cancer therapy, antibacterial treatment, and antioxidant therapy. Additionally, the theoretical foundations and technical support have been provided for the development of novel diagnostic and therapeutic strategies using CDs [15–19].

Previous metal-based nanozymes (such as iron, zinc, manganese-based, and noble metal-doped varieties) have also been shown to mimic the activity of natural enzymes, effectively scavenging ROS to alleviate oxidative stress. Additionally, they reduce the release of pro-inflammatory cytokines (e.g., Tumor Necrosis Factor-α (TNF-α), interleukin-6 (IL-6)) by inhibiting the NF-κB signaling pathway and regulating the JAK/STAT pathway. This dual-action mechanism simultaneously addresses two core pathological issues in IBD—immune dysregulation and oxidative stress—making them a highly promising new therapeutic strategy beyond traditional anti-inflammatory approaches, owing to their precisely targeted dual effects [20].

Traditional Chinese medicines (TCMs) have been extensively clinically applied and are abundant in bioactive components, showing potential for use in combating diseases. On the other hand, isolation and purification often lead to the loss of active component activity, and the bioavailability of monomers is frequently lower than that of crude extracts. More importantly, traditional Chinese medicine relies on the synergistic effects of thousands of components at specific concentrations, making it difficult to elucidate traditional dose-effect relationships [21]. However, the limitations of TCMs include low efficacy, solubility of the active ingredients, and bioavailability, as well as slow onset [22]. TCMs can be integrated with CDs as a novel approach for addressing these challenges by increasing the solubility, stability, and bioavailability of TCM components and leveraging their enzyme-mimetic activities to amplify the therapeutic effects of TCM [23].

In summary, the complex pathological network of IBD necessitates multi-target intervention. While TCM holds this potential, its application is limited by physicochemical properties. CDs offer novel approaches through catalytic therapy and precision delivery, yet their biological activity often lacks disease specificity. Therefore, the green synthesis of TCM-CDs by using TCM as a carbon source holds promise for constructing a class of "smart nanomedicine" that integrates the synergistic multi-component effects of TCM with the catalytic and delivery advantages of CDs. This strategy aims to advance IBD treatment from a "single-target" to a "systems regulation" paradigm. This review aims to systematically elucidate the classification, green synthesis strategies, and multi-mechanistic synergistic therapeutic effects of TCM-CDs, conduct an in-depth analysis of their unique challenges, and prospectively explore how AI-driven design may offer novel pathways to address these challenges.

Classification and Synthesis Methods of CDs

Classifying CDs

CDs are primarily classified into four major categories based on their core carbon structure, size, and surface chemical characteristics: graphene quantum dots (GQDs), carbon quantum dots (CQDs), carbon nanodots (CNDs), and carbonized polymer dots (CPDs) (Table 1). The differences in the structural features and properties of these CD subtypes must be understood for appropriately designing and optimizing their application as nanozymes in targeted IBD therapy.

GQDs

GQDs are nanoscale particles composed of single or few-layer (typically 1–3 layers) graphene sheets, characteristically ranging from 2 to 10 nm in size [24,25]. Their fluorescent properties primarily originate from the quantum confinement and edge effects [26]. The band gap of GQDs is tunable. The fluorescence emission of GQDs can be precisely adjusted from the ultraviolet to near-infrared region by controlling their size (2–5 nm) and surface chemical modifications, such as -OH and -COOH functional groups [27,28]. Additionally, GQDs are highly photochemical stable [29].

CQDs

CQDs are quasispherical nanoparticles consisting of an sp2-hybridized carbon core and abundant surface functional groups, typically less than 10 nm in size [30]. Their fluorescence mechanism is mainly attributed to the synergistic effect of surface state emission and quantum confinement [31,32]. The synthesis conditions and surface modifications of CQDs were optimized to achieve the fluorescence quantum yield of CQDs of at least 80% [33].

CNDs

CNDs are nanoparticles composed of amorphous carbon, characterized by short-range order and long-range disorder in their structures [34,35]. Their fluorescence properties are primarily influenced by the surface chemical com-

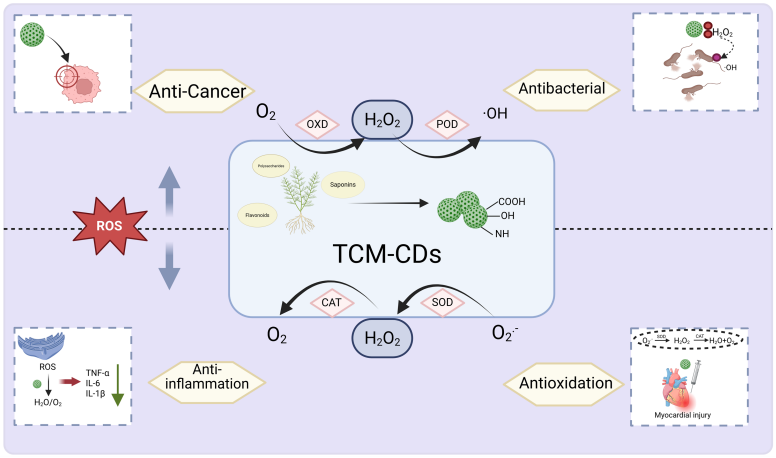

Fig. 1. Mechanisms through which TCM-CDs mimic the activity of enzymes. CDs can mimic the catalytic activities of various natural enzymes, primarily including peroxidase (POD) and oxidase (OXD), which catalyze the generation of ROS for antibacterial and anticancer therapies, and superoxide dismutase (SOD) and catalase (CAT), which are responsible for decomposing and scavenging ROS. CDs are thus suitable for anti-inflammatory and antioxidant treatments. They retain the polysaccharides, flavonoids, and saponins from the TCM-CDs carbon source, forming surface functional groups that exhibit enzyme-like activities. Created in BioRender. Huang, C. (2026) https://BioRender.com/91c8h2d.

position, such as N and S heteroatom doping, and structural defects, such as the sp^3/sp^2 carbon ratio [36]. CNDs typically exhibit broad-spectrum emission along with high photostability and biocompatibility; as such, CNDs are often suitable for biological imaging applications [37–39].

CPDs

CPDs are nanoparticles consisting of a carbon core and a large number of surface functional groups or polymer chains. CPDs have structural characteristics that are intermediate between those of CQDs and CNDs [40,41]. Their fluorescence mechanism is mainly attributed to the effects of molecular fluorophores and crosslink-enhanced emission [42]. CPDs typically exhibit excitation-wavelength-dependent fluorescence characteristics and high fluorescence quantum yields, being highly dispersible in water [43,44].

Synthesis Methods of CDs

Controlling the synthesis of CDs has been a central scientific challenge since the discovery of CDs [45,46]. The methods of preparing CDs are strongly influenced by the reaction conditions, such as temperature, pressure, pH, and reaction time, as well as the precursors used, such as small organic molecules, natural products, and polymers) [47–50]. These factors collectively determine the final structure and performance characteristics of CDs. CDs preparation methods can be categorized into two major approaches based on the carbon source and synthesis strategy: top-down and bottom-up methods [51,52].

Top-down synthesis primarily involves physically or chemically exfoliating macroscopic carbon materials, such as graphite and carbon nanotubes to produce CDs. These approaches typically involve strong oxidant treatment, electrochemical exfoliation, and mechanical exfoliation, which yield smaller CDs with well-defined structures. However, the CDs yield achieved with these methods is low, and the methods do not enable the control of the surface functional groups [53–55]. In contrast, bottom-up synthesis methods use small molecular carbon sources, such as citric acid and glucose, in molecular or ionic states as precursors, forming CDs through processes such as pyrolysis and carbonization. The precursor selection and synthesis route design of these methods are flexible, enabling precise control over the size, surface chemistry, and optical properties of the CDs [56–59]. It is well-known that in traditional medicine, Donkey-Hide (Ejiao) possesses a blood-enriching effect. The Donkey-Hide derived carbon dots (G-CDs) synthesized via a top-down method effectively retain the hematopoietic active peptide components inherent to Ejiao itself [60]. The bottom-up synthesis method for CDs is widely regarded as a green synthesis approach primarily because it aligns more closely with the principles of green chemistry—specifically in terms of raw material sources, reaction conditions, solvent use, and process energy consumption—compared to traditional top-down methods or other quantum dot synthesis techniques. Interestingly, the bottom-up approach coincides with the preparation methods of "carbonized medicine" in traditional Chinese medicine, thus giving rise to the development of TCM-CDs. Bottom-up strategies have thus received attention from researchers, driving rapid advancements in CD research. CDs with diverse characteristics and application potential have now been produced. The specific classifications of the top-down approaches for CDs are as follows (Fig. 2).

Table 1. Comparison of structural features, synthesis methods, and enzyme-like activities of different types of carbon dots (CDs).

Type	Full name	Structural features	Typical synthesis methods	Enzyme-likeActivities&KeyProperties
GQDs	Graphene Quantum Dots	Single or few-layer (1-3 layers) graphene sheets. Size: 2–10 nm. Fluorescence from quantum confinement and edge effects [24,25]. Tunable band gap via size and surface functional groups (-OH, -COOH) [27,28]. Excellent photostability and chemical stability [29].	Top-down (e.g., electrochemical exfoliation, oxidative cleavage of graphite, CNTs)	Exhibit a wide range of enzyme-mimicking activities including Peroxidase (POD), Oxidase (OXD), Superoxide Dismutase (SOD), Catalase (CAT). Valence state and surface chemistry crucial for catalytic mechanisms.
CQDs	Carbon Quantum Dots	Quasi-spherical nanoparticles with an sp^2 hybridized carbon core and abundant surface functional groups typically $<$10 nm [30]. Fluorescence from surface state emission and quantum confinement synergy [31,32]. High quantum yield (up to 80%) [33].	Bottom-up (e.g., Hydrothermal/Solvothermal, Microwave-assisted, Pyrolysis from small molecules like citric acid, glucose)	Commonly possess POD, OXD, SOD, Glucose Oxidase (GOx), Glutathione Peroxidase (GPx), and CAT activities. High catalytic versatility and biocompatibility make them suitable for therapeutic applications.
CNDs	Carbon Nanodots	Composed of amorphous carbon; short-range order and long-range disorder [34,35]. Fluorescence heavily influenced by surface chemical composition (e.g., N, S doping) and structural defects (sp^3/sp^2 carbon ratio) [36]. Exhibit broad-spectrum emission [37–39].	Varies (Bottom-up common)	Possess enzyme-like activities (e.g., POD, OXD). Valued more for excellent photostability and biocompatibility, making them ideal for bioimaging applications.
CPDs	Carbonized Polymer Dots	Feature a carbon core with numerous surface functional groups or polymer chains. Structure is intermediate between CQDs and CNDs [40, 41]. Fluorescence arises from molecular fluorophores and crosslink-enhanced emission (CEE) effect [42]. Exhibit excitation-dependent fluorescence, high quantum yield, and good water dispersibility [43,44].	Bottom-up (e.g., controlled pyrolysis/carbonization of polymers or molecular precursors)	Exhibit similar nanozyme activities to CQDs (POD, OXD, etc.). The polymer-like structure and high density of functional groups can be tailored for specific catalytic and therapeutic functions.

Hydrothermal/Solvothermal Methods

Hydrothermal and solvothermal methods are widely used for synthesizing CDs. These two methods are primarily distinguished by the reaction media used: water and organic compounds are used as the solvents in hydrothermal and solvothermal methods, respectively [61,62]. Both approaches involve the use of sealed autoclave systems to facilitate carbonizing and functionalizing the precursors under elevated temperature and pressure. These methods offer several advantages, such as operational simplicity, mild reaction conditions, and high reproducibility, enabling the precise control over the size distribution; morphology (spherical, sheets, etc.); and surface chemistry, such as the types and densities of functional groups, of CDs [63,64].

The small-molecule precursors of CDs undergo complex chemical transformations during the reaction process. The initial dehydration and condensation reactions are followed by intermolecular crosslinking to form carbon chain frameworks, culminating in carbonization at elevated temperatures to yield CDs with specific structures [65,66]. This process forms π–π*-conjugated systems and surface functional group modifications, which are key in influencing the optical properties and enzyme-like activities of the resulting CDs [67]. Huang *et al.* [68] used the TCM herb Bletilla striata as a precursor to hydrothermally synthesize green-fluorescent CDs (BS-CDs) with a uniform size distribution (3.5 ± 0.6 nm). BS-CD treatment alleviated clinical symptoms and pathological damage in the colon of mice with ulcerative colitis in a dextran sulfate sodium (DSS)-induced colitis mouse model. These effects were potentially mediated by reduced levels of myeloperoxidase (MPO), TNF-α, interleukin-1 beta (IL-1β), and IL-6.

Microwave-Assisted Synthesis

Microwave-assisted synthesis is a highly efficient and rapid methodology for preparing CDs with advantages including a shortened reaction time, high yield, low energy consumption, and precise control over CDs characteristics [69]. This technique involves the use of microwave irradiation to rapidly and uniformly heat the precursor materials, accelerating the carbonization and functionalization processes, often synthesizing CDs within minutes [70]. The dielectric heating effect generated by microwave radiation enables selective molecular-level heating, facilitating the formation of CDs with a uniform size distribution and homogeneous surface functional groups [71]. Jiang *et al*. [72] used neutral red and levofloxacin as precursors to synthesize novel RNA-targeting red-emitting CDs (M-CDs) with microwave assistance. The quantum yield of the resulting M-CDs was 22.83%. The M-CDs demonstrated high RNA-selective binding capability, producing strong red fluorescence enhancement. The M-CDs displayed ultrafast cellular uptake and internalization, within 5 s, providing a tool for the real-time imaging of stress granule dynamics under oxidative stress conditions. Li *et al*. [73] prepared ginger-derived CDs (GCDs) using an aqueous ginger extract as a precursor and a microwave-assisted hydrothermal method at 180 °C. The synthesized GCDs exhibited a narrow size distribution (average diameter: 2.3 nm), intense blue photoluminescence, and high biocompatibility. The GCDs showed suitability for in vitro bioimaging as well as anti-inflammatory activity, accelerating wound healing processes. GCDs have shown antimicrobial activity and potential for sensor applications [74,75].

Thermal Decomposition

Thermal decomposition is another crucial technique for synthesizing CDs. This method involves subjecting precursors to high-temperature treatment, typically 300–1000 °C, under an oxygen-free or inert atmosphere such as N_2 or Ar, facilitating pyrolysis and carbonization processes [76,77]. Organic molecules undergo complex chemical reactions, including dehydration, decarboxylation, and aromatization, during thermal decomposition, forming nanostructures with sp^2/sp^3-hybridized carbon cores and surfaces rich in oxygen- and nitrogen-containing functional groups such as -COOH, -OH, and -NH_2 [78]. Zhang *et al*. [79] developed a sustainable green synthesis strategy using rhubarb as a precursor to prepare rhubarb–CDs via high-temperature pyrolysis (350 °C). These CDs had a uniform size distribution, a surface rich in bioactive groups, and multiple biological activities for treating UC. The Rhubarb-derived Carbon Dots promote rapid hemostasis through increasing platelet aggregation, producing anti-inflammatory effects via inhibiting the nuclear factor-κB (NF-κB) signaling pathway, protecting antioxidants through ROS scavenging, and effectively maintaining the barrier function of the intestinal mucosa. Wang *et al*. [80] used kudzu root (P. lobatae Radix, PLR) as a raw material to prepare novel CDs via pyrolysis. These CDs reduced serum uric acid levels by inhibiting xanthine barrier function activity, offering insights into treating hyperuricemia.

TCM-CDs: Nanopharmaceutical Platforms for Treating IBD

This section focuses on CDs derived from TCM based on the above-described systematic classification of and strategies for synthesizing CDs. This section describes the screening of active ingredients from TCM prior to synthesizing TCM-CDs, the synthesis process, and the therapeutic mechanisms of TCM-CDs, such as potent ROS scavenging, synergistically regulating the gut microbiota, and the modulation of inflammatory signaling pathways (Table 2).

Strategies for Designing CDs Derived from TCM

Although TCM-CDs possess SOD, CAT, and other enzyme-mimetic activities, most TCM-CDs are in the early stages of development. A specific method of designing TCM-CDs is lacking. The catalytically active sites in nanozymes have been precisely engineered via modulating the surface electronic structure, introducing heteroatom dopants, and tuning the edge defect density in CDs. The enzyme-mimetic properties of CDs are generally created using pristine CDs, which intrinsically mimic enzymes; CDs functionalized via heteroatom doping; or hybrid nanozymes constructed via integrating CDs with other functional materials [7]. TCM precursors are intrinsically rich in phenolic hydroxyls, quinones, alkaloids, and other structural motifs that can be thermally converted into conjugated sp^2 domains, C–N/C=N linkages, or metal coordination sites during carbonization, providing natural templates for the in situ construction of catalytic centers. Furthermore, multiple parameters—including charge, particle size, and surface modification—are intimately involved in the preparation methods of different nanoparticles. Consequently, the design and fabrication process must carefully consider the nanoparticles' compatibility, stability, biological activity, and safety [81].

CDs are primarily composed of carbon, hydrogen, and oxygen; hetero-elements such as sulfur, nitrogen, and phosphorus are frequently incorporated into these CDs to modulate their properties. Moreover, metal-containing CDs, such as Fe-, Cu-, or Ni-doped CDs, are commonly synthesized to enhance their intrinsic catalytic activity. Consequently, the type of precursor substrate can be deliberately varied during the design phase to achieve heteroatom doping, enabling the precise control of the elemental composition of the resulting CDs [82]. Cui *et al*. [83] synthesized iodine–copper–zinc ternary-doped carbon dots (Cu, Zn, I-CDs) by introducing metal ions during carbonization. These dots exhibited simultaneous CAT-, SOD-, and glutathione peroxidase-mimetic activities, enabling the scavenging of overproduced ROS for UC therapy. Additionally

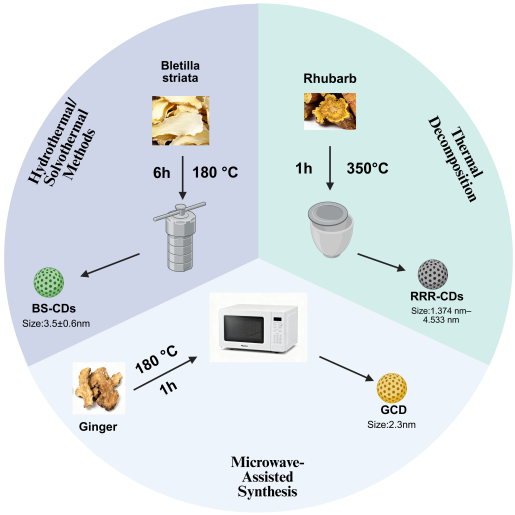

Fig. 2. Classification and synthesis of TCM-CDs. Bottom-up (e.g., hydrothermal/solvothermal, microwave-assisted synthesis, pyrolysis) methods use TCMs as carbon sources, undergoing carbonization and functionalization under specific conditions to produce CDs with defined size, surface chemistry, and bioactivities.Created in BioRender.Huang, C. (2026) https://BioRender.com/gmqallg.

I doping endowed Cu, Zn, and I-CDs with enhanced triple-antioxidant nanozyme activity compared with that of Cu, Zn-CDs. Gao *et al*. [84] used Scutellaria barbata (SB) and Herba Hedyotis diffusae (HHD) as precursors to fabricate SB–HHD–CDs via a one-step hydrothermal method. These CDs are less expensive, free from selenium and metals, and do not have the intrinsic cytotoxicity associated with conventionally doped CDs. The antioxidant performance of these CDs was comparable to or superior to that of their counterparts, notably exhibiting robust SOD-mimetic activity. Nie *et al*. [85] engineered dynamic ROS nanoregulators derived from TCM-CDs by tailoring their surface states for the on-demand treatment of inflammation or infection eradication. Three distinct CDs were synthesized: honeysuckle-, dandelion-, and taxus leaf-derived CDs (HOCDs, DACDs, and TACDs, respectively). The HOCDs selectively scavenged harmful ROS, TACD generated bactericidal ROS upon photodynamic activation, and DACDs exhibited anti-inflammatory and antimicrobial effects, acting as a dynamic modulator of infectious chronic inflammatory conditions.

In summary, CDs with enzyme-mimetic activities can be developed on demand through flexibly manipulating heteroatom doping, using TCM precursors as natural templates, and precisely regulating surface chemistry.

Screening and Advantages of TCMs as Carbon Sources

The active ingredients in TCMs with the potential for treating IBD must be precisely screened to serve as carbon sources. This strategy can reveal the mechanism through which TCM-CDs act in treating IBD, which can guide the development of efficient targeted CD nanomedicines for IBD [86]. The screening process must be specifically designed based on the core pathological features of IBD, such as chronic inflammation, oxidative stress, and intestinal barrier damage [87]. TCMs are rich in specific bioactive molecules such as polyphenols, alkaloids, and flavonoids, and are thus suitable carbon sources. The screening criteria should focus on the inherent potent anti-inflammatory and antioxidant properties of candidate TCM components [88]. The possible synergistic effects of the conversion of TCMs into CDs must be prospectively evaluated, for example, increasing the solubility and bioavailability of the original drug, endowing or enhancing nanozyme activity, and strengthening the targeting ability. These evaluations are required to ensure that the final TCM-CDs accurately intervene in the complex pathological network of IBD.

Tanshinone IIA is a bioactive compound extracted from *Salvia miltiorrhiza* (Danshen) has been highlighted in in-depth studies of TCMs for treating IBD [89]. Tanshinone IIA exerts therapeutic effects via modulating the NF-κB signaling pathway, effectively alleviating IBD symptoms, demonstrating substantial potential as a therapeutic agent for managing IBD. The traditional Chinese herb, Coptis chinensis (Chinese gold thread), has similarly attracted attention. Berberine is a classic isoquinoline alkaloid derived from this plant, has emerged as a research hotspot. Zhu *et al*. [90] leveraged the distinctive pharmacological properties of berberine to effectively treat UC through modulating the IL-6/signal transducer and activator of transcription 3 (STAT3)/NF-κB signaling pathway, providing novel perspectives and methodologies for IBD therapeutics. Curcumin is a natural polyphenolic compound derived from the rhizomes of Curcuma longa (turmeric) of the Zingiberaceae family. Curcumin has important pharmacological properties, including anti-inflammatory, antioxidant, and antiproliferative activities. Curcumin has shown ther-

apeutic potential in managing IBD [91]. Mechanistically, curcumin targets multiple proinflammatory signaling pathways through suppressing the expression of key inflammatory mediators such as cyclooxygenase-2 (COX-2), lipoxygenase (LOX), TNF-α, interferon-γ (IFN-γ), and NF-κB. This modulation effectively blocks inflammatory cascades, attenuating intestinal mucosal damage, inhibiting inflammatory cell infiltration, reducing the colon weight-to-length ratio, and increasing survival rates [92,93]. The chemical stability and natural availability of curcumin confer distinct advantages over conventional synthetic anti-inflammatory agents, such as lower production costs and fewer adverse effects during long-term administration [94].

Active ingredients, such as berberine and curcumin, along with their derivatives and structural features, are likely retained or transformed during carbonization, endowing the resulting CDs with biological activities highly relevant for treating IBD. Gambogic acid is a natural anti-tumor compound, but its clinical translation is limited due to poor water solubility, significant toxic side effects, and low targeting ability. To overcome these limitations, Qiu *et al*. [95] developed M@GaGaNPs, achieving the dual effects of precision therapy and immune activation. This constitutes an innate advantage of TCM-CDs over ordinary or chemically synthesized CDs.

Green TCM-CD Preparation Strategies

Herbal CDs are primarily synthesized via top-down approaches, including hydrothermal and solvothermal, microwave-assisted, and pyrolytic methods. The core objectives of these methods for preparing TCM-CDs, regardless of the approach used, are maximizing the retention or transformation of active groups/structures derived from TCMs such as phenolic hydroxyl groups, quinone structures, and nitrogen-containing heterocycles; and producing nanozyme activity via regulating temperature, time, and precursor treatment.

HOCDs and DACDs are rich in phenolic hydroxyl groups and exhibit ROS-scavenging capacities. The surfaces of DACDs and TACDs contain C–N/C=N bonds; DACDs and TACDs possess a band structure that favors absorption in the red region and facilitates $O_2{\bullet}^-$ generation during light-induced sterilization [85]. Patel *et al*. [96] used banana peel waste as a raw material to synthesize banana peel carbon dots (BCDs) via a hydrothermal method. Deionized water and ethanol were mixed in a 1:1 ratio, and the reaction was conducted at 200 °C for 24 h. Curcumin was combined with the BCDs: the hydroxyl peaks of the BCDs were stretched, the C=C bonds extended, and the olefin double bonds conjugated with aromatic rings, resulting in stronger antibacterial and antioxidant activities. Architha *et al*. [97] synthesized CQDs from Ocimum basilicum (Mexican mint) using a microwave-assisted method. FT-IR spectroscopy confirmed the presence of various functional groups, such as -OH, -CH, C=O, and C-O, in the CQDs. CDs were successfully prepared via the high-temperature calcination of Artemisia argyi leaves in a muffle furnace, with -OH, C≡N, and C=O groups present on the CD surfaces. These CDs produced antifrostbite effects, potentially achieved by reducing the concentrations of IL-1β and TNF-α. Although these CDs were easy to prepare, the preparation process potentially negatively impacted the pharmacological activities of the TCMs [98]. Deng *et al*. [91] compared honeysuckle CDs synthesized via carbonization and hydrothermal methods. Both CDs had surface groups including -OH, -NH_2, and -COOH. However, the honeysuckle CDs synthesized via the hydrothermal method (Hy-CDs) were rich in -NH_2 on the surface, exhibiting stronger SOD enzyme activity and lower TNF-α, IL-1β, and IL-6 levels.

Unique Mechanisms of Traditional Chinese Medicine-Derived Carbon Dots in IBD Treatment

Intrinsic Antioxidant Activity and ROS Scavenging

The reactive ROS-mediated disruption of redox homeostasis in small intestinal epithelial cells can be therapeutically targeted using nanozymes via ROS scavenging, achieving IBD remission [99] (Fig. 3). CDs combined with TCMs enhance the pharmacological activity of small TCM molecules and retain the functional groups relevant to disease treatment, such as the hydroxyl, carboxyl, carbonyl, and amino groups [23]. Yang *et al*. [100] used Lophatherum gracile (bamboo leaf) as the carbon precursor to synthesize highly stable CDs using a green strategy. These nanostructures retained the phenolic hydroxyl groups (-OH) from the natural precursor, which exhibited potent antioxidant activity. The CDs efficiently neutralized hydroxyl radicals (•OH) and superoxide anions ($O_2{\bullet}^-$) through electron transfer mechanisms, thereby ameliorating oxidative stress-induced damage. Notably, Lonicera japonica (honeysuckle)-derived CDs mitigated cellular inflammation via eliminating ROS, as evidenced in pulmonary injury and lung ischemia–reperfusion models [91]. Based on the pathological characteristics of IBD, stimulus-responsive drug delivery nanoplatforms can be utilized, in combination with AI-driven design, to develop carrier materials that are responsive to ROS, thereby achieving targeted drug release [101].

Synergistic Regulation of Intestinal Flora

Another pathological hallmark of IBD is gut dysbiosis, in which the intestinal microbiota plays a pivotal role in disease progression. Natural polysaccharides derived from TCMs are fermented by gut microbiota, maintaining intestinal flora homeostasis by promoting the proliferation of probiotics and inhibiting the growth of harmful bacteria [102]. Simultaneously, they improve microbial metabolism and repair mucosal barrier function, offering unique advantages for IBD treatment. The TCMs used for treating IBD con-

tain components such as polyphenols and alkaloids, which produce antibacterial and anti-inflammatory effects. The unstable and poorly water-soluble active ingredients can be converted into CDs to achieve a synergistic effect for treating IBD. Curcumin-derived CDs are a novel class of antimicrobial agents that demonstrate broad-spectrum antibacterial activity in animal models at elevated minimum bactericidal concentrations. These CDs effectively inhibit Gram-positive and Gram-negative bacilli while exhibiting suitable physicochemical properties, including aqueous solubility, biocompatibility, low cytotoxicity, and intrinsic fluorescence, for medical application [103,104]. Berberine is an active component of the traditional Chinese medicine Coptis chinensis that exhibits antibacterial, anti-inflammatory, and antioxidant properties. The increased intestinal microbial abundance and community diversity of mice treated with roasted Coptis chinensis CDs were higher than those of mice treated with DSS, indicating that the roasted Coptis chinensis CDs regulated the flora of mice with DSS-induced colitis [105].

Targeted Regulation of Inflammatory Signaling Pathways

The pathological progression of IBD is closely associated with the aberrant activation of critical signaling pathways, such as the NF-κB and NLRP3 pathways. Herbal-derived CD nanozymes reduce the inflammation in multiple targets through modulating these pathways. For instance, Sophora flavescence-derived CDs ameliorated ethanol-induced gastric mucosal injury via downregulating NF-κB signaling, thereby reducing the levels of downstream proinflammatory cytokines such as TNF-α and IL-6 [106]. Furthermore, Berberine-derived Carbon Dots (Ber-CDs) exhibit a two regulatory mechanism in 5-fluorouracil-induced colitis models: suppressing NLRP3 inflammasome assembly to block pathway activation and rebalancing macrophage polarization. These processes indicate a negative correlation between proinflammatory IL-1β and anti-inflammatory interleukin-10 (IL-10) levels, confirming their bidirectional modulation capability within inflammatory microenvironments [107]. In a Lipopolysaccharide (LPS)-induced acute inflammation mouse model, carbon dots derived from purple sweet potato-derived carbon dots (CPP-CDs) demonstrated excellent performance by inhibiting the TLR4/NF-κB pathway and regulating the NLRP3 inflammasome, thereby exerting anti-inflammatory effects [108].

The Therapeutic Network of Multi-Mechanistic Synergistic Effects

The aforementioned three major therapeutic mechanisms of TCM-CDs do not function in isolation; instead, they constitute an organic, synergistic, and mutually reinforcing therapeutic network (Fig. 3). Taking sepsis as an example, researchers have proposed and validated the "multi-target synergistic therapy" strategy—given that sepsis involves cytokine storms, oxidative stress outbursts, and multi-organ dysfunction, single-target drugs often exhibit limited efficacy. In contrast, a nanodelivery system integrating antibacterial, anti-inflammatory, and antioxidant functions has demonstrated significant therapeutic advantages [109]. This concept offers important insights for the treatment of IBD: IBD is likewise a complex disease driven by the interplay of gut microbiota dysbiosis, immune dysregulation, and oxidative damage. As a novel type of nanomaterial that integrates medicine and excipient, TCM-CDs inherently possess multiple activities—antibacterial, anti-inflammatory, and antioxidant—and are thus expected to play a key role within this "triple-action" therapeutic framework.

Specifically, the potent ROS-scavenging ability of TCM-CDs directly mitigates oxidative stress-induced damage to intestinal epithelial cells, laying the foundation for intestinal barrier repair. At the same time, this creates a microenvironment less conducive to the growth of pro-inflammatory microbiota. Additionally, an imbalance in the relative levels of pathogenic and beneficial bacteria may also contribute to the persistence of IBD [110]. Therefore, modulating the gut microbiota through direct antibacterial effects or by promoting the growth of beneficial bacteria not only competitively inhibits pathogens, but also—through their metabolites (such as short-chain fatty acids)—further strengthens intestinal barrier function and directly exerts anti-inflammatory effects, thereby assisting in the regulation of immune responses [101]. Ultimately, the inhibition of key inflammatory pathways such as NF-κB and JAK/STAT curbs the inflammatory cascade at its signaling source, reducing inflammatory cell infiltration and cytokine storms. This, in turn, helps restore intestinal homeostasis and normal redox balance. For example, Cimicifuga Carbon Dots (CR-CDs) synthesized via pyrolysis exhibit SOD- and CAT-like enzyme activities. They not only effectively scavenge reactive oxygen species but also inhibit the levels of TNF-α and IL-6, activate the Nrf2/HO-1 antioxidant signaling pathway, and balance the gut microbiota—suppressing pathogenic bacteria while increasing beneficial bacteria [111]. This "antioxidant-microbiota-modulating-anti-inflammatory" triple-action synergy enables TCM-CDs to more comprehensively intervene in the complex pathological cycle of IBD, underscoring their significant advantage over single-target drugs.

Limitations and Future Challenges of TCM-CDs in Treating IBD

Despite the environmental sustainability, cost-effectiveness, and therapeutic efficacy of TCM-CDs, TCM-CDs face challenges in terms of long-term toxicity, the lack of knowledge of their metabolic pathways, and clinical translation.

Table 2. TCM-CDs: from herbal precursors to multi-target nanotherapeutics for IBD.

TCM active ingredient	Original bioactivity	CDs preparation & Structural features	retained/enhanced functions after carbonization	core mechanisms for IBD therapy	Structure-function retention & Stability mechanism
Tanshinone IIA (from Salvia miltiorrhiza)	Exerts anti-inflammatory effects by modulating the NF-κB signaling pathway, alleviating IBD symptoms [89].	Specific preparation method not detailed in the text. The CD structure is anticipated to retain the quinone active center.	Retains the ability to modulate the NF-κB pathway and may enhance its stability and bioavailability via the nano-form.	Inhibits the NF-κB inflammatory signaling pathway, reducing intestinal inflammation [89].	The quinone structure serves as a key pharmacophore and electron transporter. Its stability within the carbon core post-carbonization is the structural basis for the retained anti-inflammatory activity.
Berberine (from Coptis chinensis)	Antibacterial, anti-inflammatory, antioxidant. Treats UC by modulating the IL-6/STAT3/NF-κB pathway [90,105].	Carbonized from roasted Coptis chinensis. The resulting CDs (SCR-CDs) are rich in surface nitrogen-containing functional groups [105].	1. Significantly regulates gut microbiota: Increases microbial abundance and diversity. 2. Enhances anti-inflammatory activity: Achieves bidirectional anti-inflammatory effects by modulating inflammatory pathways (e.g., NLRP3) and macrophage polarization [105,107].	1. Corrects DSS-induced gut dysbiosis [105]. 2. Inhibits NLRP3 inflammasome activation, balances macrophage phenotypes, and reduces pro-inflammatory cytokines like IL-1β [107].	The nitrogen-containing heterocycle structure of the isoquinoline alkaloid is transformed into stable C-N/C=N structures post-carbonization. These structures are not only the basis for antibacterial and anti-inflammatory activities but may also form enzyme-like catalytic centers, conferring new biological functions.
Curcumin (from Curcuma longa)	Anti-inflammatory, antioxidant, anti-proliferative. Exhibits therapeutic potential by inhibiting multiple targets like COX-2, LOX, TNF-α, IFN-γ, NF-κB [92–94].	Complexed with banana peel CDs (BCDs). Post-carbonization, its phenolic hydroxyl groups and C=C bonds are retained and extended, with an enhanced conjugate system [96].	1. Significantly enhances water solubility, stability, and bioavailability. 2. Gains potent broad-spectrum antibacterial activity (against Gram-positive and Gram-negative bacteria). 3. Antioxidant capacity is enhanced [96,103,104].	1. Modulates gut microbiota via direct bactericidal effects. 2. Efficiently scavenges ROS, alleviating oxidative stress. 3. Multi-target inhibition of inflammatory pathways.	Phenolic hydroxyl groups (-OH) and the olefin-aromatic conjugate system are key to curcumin's antioxidant activity. Under mild carbonization conditions (e.g., hydrothermal method), these groups are stably retained on the CD surface or within the structure, which is the fundamental reason for the retention and enhancement of its function.
Polyphenols (e.g., from Taraxacum mongolicum, Lonicera japonica)	Antioxidant, anti-inflammatory.	Synthesized via hydrothermal method. CDs surface is rich in -OH, -COOH and other functional groups (e.g., Hy-CDs are rich in $-NH_2$) [85, 91].	Potent ROS scavenging ability: Retains and enhances the precursor's antioxidant activity, and may possess enzyme-like activities such as SOD [91].	Directly neutralizes free radicals like -OH and $O_2^{\bullet -}$, ameliorates oxidative stress damage, and protects intestinal epithelial cells [91,100].	Phenolic hydroxyl groups (-OH) possess high stability and are the direct active sites for ROS scavenging by CDs. Their abundant retention during carbonization is the most direct manifestation of the "structure-function" relationship. The hydrothermal method better preserves active groups like $-NH_2$ [91].
Alkaloids/N-containing compounds (e.g., from Sophora flavescens, Coptis chinensis)	Antibacterial, anti-inflammatory, regulates signaling pathways.	Synthesized via solvothermal method, etc. C-N/C═N structures are formed on the CD surface [85].	Gains enzyme-like catalytic functions: Modulates the band structure, enabling the generation of $O_2^{\bullet -}$ under light for sterilization, or mimicking enzymes like SOD to scavenge ROS [85].	1. Photocatalytic sterilization modulates flora. 2. Scavenges ROS via enzyme-like activities such as SOD.	Nitrogen-containing precursors form stable C-N/C=N structures during carbonization. This structure effectively modulates the band structure of the CDs, forming the electronic basis for their oxidase (OXD)-like or antioxidant enzyme (SOD)-like activity.

TCM, Traditional Chinese medicine; CDs, carbon dots; IBD, inflammatory bowel disease; DSS, dextran sulfate sodium; NLRP3, NOD-Like Receptor Pyrin Domain-Containing Protein 3; UC, Ulcerative colitis; SCR-CDs, Roasted Coptis chinensis Carbon Dots; reactive oxygen species; SOD, Superoxide Dismutase.

Defects in Material Synthesis: Structural Heterogeneity

TCM-CDs can be synthesized using various methods. The different temperatures, synthesis durations, and pretreatment procedures of the methods result in differences in the surface groups on the synthesized CDs, leading to variations in enzymatic activity. Preparing TCM-based nanozymes requires the careful selection of active ingredients and the removal of excess impurities and nonessential components because TCMs contain multiple components. Moreover, during TCM-based nanozyme synthesis, the physicochemical properties must be optimized to ensure high enzymatic activity, long-term stability, and the expected pharmacological effects [112]. In addition to the issues of structural heterogeneity and uncontrollable enzyme-like activity, the low retention rate of active ingredients must be addressed. Green synthesis methods mainly involve synthesizing CDs at high temperatures. However, strict monitoring and control are required to ensure the activity of the raw TCM materials is retained after high-temperature treatment, and studies are needed to determine whether byproducts are generated during the process. This provides an opportunity for the intervention of AI. By leveraging machine learning to uncover hidden patterns within high-throughput data, it holds the potential to achieve the rational design and performance prediction of TCM-CDs.

Biological Uncertainty: Unclear Metabolism

TCM has attracted attention from researchers owing to the potential for using TCM in areas such as antioxidant therapy, inflammation regulation, and neuroprotection, which is attributed to the ROS-scavenging ability of many TCMs [113]. However, the metabolic behavior of TCMs, which is a key factor affecting their practical application, also requires in-depth study. The metabolic kinetics of nanozymes not only directly determine their pharmacokinetic characteristics, including in vivo half-life, tissue-specific distribution, and clearance rate, but also the biocompatibility and toxicity of intermediates or decomposition products potentially generated during metabolism, which are core parameters for evaluating the long-term safety of the materials [114]. Similarly, challenges remain in optimizing drug loading and release, as well as in addressing regulatory issues [115].Therefore, the *in vivo* metabolic fates and the biological effects of the toxic metabolites of TCMs must be systematically evaluated to promote the clinical translation of TCM-CDs.

Barriers to Clinical Translation: Gap between Animals and Humans

The primary route of administering nanoparticles is intravenous injection, which enables systemic delivery. Although this approach may provide immediate symptom relief in certain situations, in the context of chronic disease treatment, it is necessary to consider both the dosage per administration and the dosing interval in order to achieve optimal therapeutic outcomes [116]. Appropriate administration methods, such as gavage or voluntary ingestion for oral administration and intraperitoneal or intravenous routes for injection, must be identified for each TCM-CDs treatment to maximize efficacy and ensure high biosafety. Different administration strategies may strongly affect the biodistribution, metabolic behavior, and toxicity of nanozymes. Therefore, the administration route must be optimized by combining the material properties, target indications, and in vivo metabolic kinetics. This research will not only help to increase the efficacy and safety of TCM-CDs but also promote the clinical translation of TCM-CDs by increasing the predictability of the use of TCM-CDs. The findings will serve as an important link in realizing the transition from experimental research to clinical application [117]. In addition, the yield of TCM-CDs is relatively low. For example, the yield of Ligusticum chuanxiong carbon dots was relatively similar, at approximately 10%, regardless of the synthesis method [118]. Although synthesizing TCM-CDs is relatively simple, the preparation process has strict requirements on experimental equipment, reaction conditions, and subsequent characterization and detection technologies. In addition, the required subsequent processing procedures, such as purification steps, may lead to a substantial increase in overall cost.

Future Outlook: Design Integrating Artificial Intelligence

Integrating AI with TCM-CDs is driving a paradigm shift in IBD management, enabling the development of precise and personalized therapeutic strategies and promoting the translation of these nanozymes from the laboratory to the clinic.

Precise AI-Driven Molecular Design

Although TCM-CDs show potential for treating IBD, further development is facing the above-mentioned challenges. AI technology has provided a tool to solve these problems and avoid traditional R&D paradigms (Fig. 4). The key problem with TCM-CDs is their black-box characteristics: the precursor components are complex, and the synthesis involves numerous parameters. The structure–activity relationships of TCM-CDs remain unclear. AI technologies, particularly machine learning and deep learning, can be used to efficiently process complex high-dimensional and nonlinear data. Machine learning is a subdiscipline of AI in which computer algorithms use statistical models to learn associations, for example, within provided datasets such as Dragon Dictation, SPAM detection, and Netflix recommendation systems, thereby showing predictive capabilities [119]. Deep learning is a prominent area in the current ML field, with the core being the deep neural network. The DNN draws on the connection patterns of neurons in the human brain and the logic of information transmission. DNNs used multilayered pro-

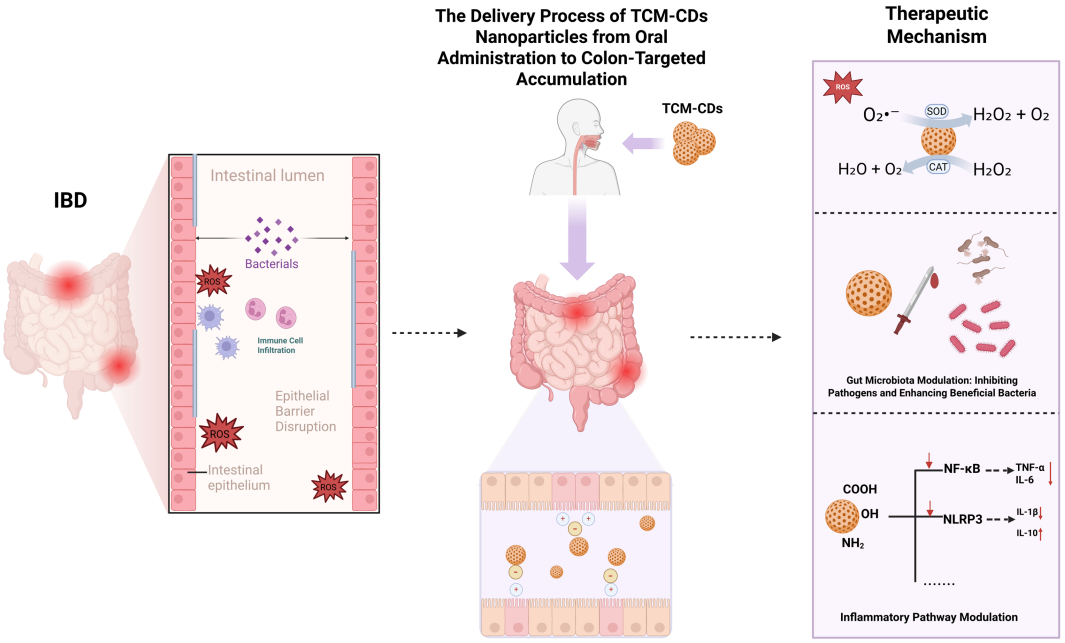

Fig. 3. Schematic illustration of the multi-mechanism synergistic action of TCM-CDs in IBD therapy. This figure comprehensively illustrates the multi-mechanism synergistic therapeutic effects of TCM-CDs against IBD. The graphic sequentially depicts, from left to right: the pathological intestinal microenvironment in IBD, the oral delivery and targeting process of TCM-CDs, and their multifaceted therapeutic actions at the disease site. TCM-CDs alleviate oxidative stress by scavenging ROS via SOD/CAT-mimetic activities, correct dysbiosis by modulating gut microbial balance, and reduce immune-inflammatory responses by inhibiting key signaling pathways such as NF-κB/NLRP3, thereby synergistically promoting the repair of the intestinal mucosal barrier. Created in BioRender. Huang, C. (2026) https://BioRender.com/jo53w2u.

cessing to automatically extract key information from data such as identifying edges in images or capturing semantic meaning from text. Deep learning does not need manually predesigned features and can accurately interpret data, assisting with complex tasks such as image recognition and language comprehension [120]. Through high-throughput techniques and AI, the specific design and optimization of lipid nanoparticles (LNPs) have been achieved, addressing the time-consuming and labor-intensive nature of traditional approaches [121].

AI models can be trained by establishing a large database containing the chemical components of TCM precursors, synthesis process parameters (temperature, time, pH, etc.), structural characteristics of CDs (size, functional groups, and doping elements), and in vitro and *in vivo* efficacy and toxicity data. The ultimate goal is reverse efficacy-oriented design: the desired therapeutic effects, such as targeted inhibition of NLRP3, efficient scavenging of ROS, could be input to the AI model, which could recommend the optimal TCM precursors and synthesis schemes. This scheme could markedly shorten the research and development cycle and reduce trial-and-error costs. Liu *et al.* [122] proposed an AI-driven inverse design approach for a drug delivery platform that spans from molecular chaperone screening to hierarchical supramolecular construction, achieving the co-assembly of baicalin and tranexamic acid.

TCM is profound and extensive, and the precursors derived from Chinese herbs are highly complex. However, based on existing clinical experience in traditional Chinese medicine and ancient texts, the theory of "monarch-minister-assistant-guide" enables multi-herb synergy to optimize therapeutic efficacy. By leveraging AI to mine literature data and optimize synthesis parameters in real time, new directions emerge for the design of multifunctional TCM compound formulas, enhancing both therapeutic outcomes and product consistency [123].

Enabling Clinical Precision Therapy

Combining AI and TCM-CDs will hopefully guide the development of personalized precision medicine for patients. The proposed AI-driven endo-histo-omics framework and the core concept of intestinal barrier repair, integrating clinical, endoscopic, histological and molecular data, could improve IBD management, enabling accurate

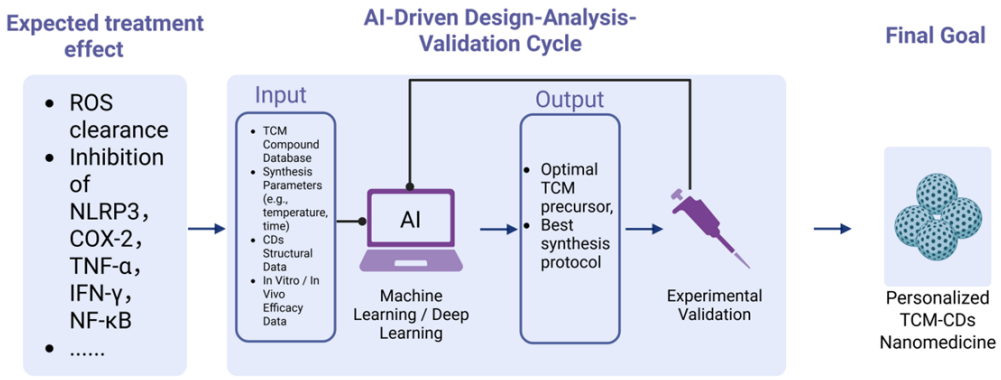

Fig. 4. Workflow of artificial intelligence (AI)-assisted design of TCM-CDs. This framework involves a closed-loop optimization process where AI powers the rational design of TCM-CDs. Data on TCM precursors, synthesis parameters, CD structural properties, and in vitro and *in vivo* efficacy and toxicity are incorporated into a central database, from which machine learning and deep learning models decipher complex structure–activity relationships. This process enables reverse efficacy-oriented design. The experimental results and new data are fed back into the AI system, creating an iterative cycle for continuous refinement and enhancing nanozyme performance. Created in BioRender. Huang, C. (2026) https://BioRender.com/jsdmgjy.

patient stratification and outcome prediction [124]. Future studies should focus on developing multifunctional CD nanozyme platforms. These platforms could be integrated with AI and multiomics technologies and a collaborative big data approach could be adopted to advance toward precision medicine for IBD [125]. Simultaneously, integrating intestinal organoid technology to model IBD pathology, in combination with organ-on-a-chip platforms, will enhance the reliability of preclinical studies and reduce reliance on animal experiments. By using AI as a bridge, TCM-CDs can be better aligned with clinical applications, thereby promoting the further advancement of TCM-CDs [126].

Conclusions

TCM-CDs provide promising therapeutic platforms for treating IBD. TCM-CDs effectively address the core pathological features of IBD, including oxidative stress, gut dysbiosis, and chronic inflammation, by leveraging the bioactivities of TCM components and the versatile catalytic functions of CDs. Green synthetic approaches enable the retention and enhancement of bioactive functional groups of TCMs, endowing TCM-CDs with superior antioxidant, antibacterial, and anti-inflammatory properties than traditional treatments.

However, the adoption of TCM-CDs faces several challenges, including structural heterogeneity, low active ingredient retention, unpredictable metabolic behaviors, and difficulties in clinical translation such as administration route optimization and industrialization costs. Future efforts should focus on standardizing the synthesis protocols, identifying the *in vivo* metabolic pathways through which TCM-CDs function, and conducting well-designed preclinical and clinical studies.

AI could be applied to overcome these barriers. AI-driven molecular design and multiomics-based patient stratification have potential for developing precision therapy, enabling the reverse design of TCM-CDs with tailored therapeutic effects and minimal side effects.

In summary, TCM-CDs not only bridge the gap between traditional medicine and modern nanotechnology but also open new avenues for the development of safe, effective, and personalized nanomedicines for IBD.

List of Abbreviations

5-FU, 5-Fluorouracil; AI, Artificial Intelligence; BCDs, Banana Peel Carbon Dots; Ber-CDs, Berberine-derived Carbon Dots; BS-CDs, Bletilla striata Carbon Dots; CAT, Catalase; CDs, Carbon Dots; CNDs, Carbon Nanodots; COX-2, Cyclooxygenase-2; CPDs, Carbonized Polymer Dots; CPP-CDs, purple sweet potato derived carbon dots; CQDs, Carbon Quantum Dots; CR-CDs, Cimicifuga Carbon Dots; Cu,Zn,I-CDs, Iodine–copper–zinc ternary-doped carbon dots ; DACD, Dandelion-derived; DL, Deep Learning; DNN, Deep Neural Network; DSS, Dextran Sulfate Sodium; G-CDs, Donkey-Hide Gelatin derived carbon dots; GCD, Ginger-derived Carbon Dots; GOx, Glucose Oxidase; GPx, Glutathione Peroxidase; GQDs, Graphene Quantum Dots; HHD, Herba Hedyotis diffusae; HOCD, Honeysuckle-derived Carbon Dots; Hy-CDs, Lonicera japonica-derived Carbon Dots; IBD, Inflammatory Bowel Disease; IFN-γ, Interferon-γ; IL, Interleukin; IL-10, interleukin-10; IL-1β, interleukin-1 beta; IL-6, interleukin-6; LC-CDs, Ligusticum chuanxiong Carbon Dots; LNPs, lipid nanoparticles; LOX, Lipoxygenase; LPS, Lipopolysaccharide; M-CDs, RNA-targeting red-emitting Carbon Dots; ML, Machine Learning; MPO,

myeloperoxidase; M@GaGaNPs, GA/Ga^{3+} nanoparticles; NF-κB, Nuclear Factor Kappa-B; NLRP3, NOD-Like Receptor Pyrin Domain-Containing Protein 3; OXD, Oxidase; PLR, P. lobatae Radix; POD, Peroxidase; ROS, Reactive Oxygen Species; RRR-CDs, Rhubarb-derived Carbon Dots; RSFC-CDs, Sophora flavescens-derived Carbon Dots; SB, Scutellaria barbata; SB–HHD–CDs, Scutellaria barbata and Herba Hedyotis diffusae-derived Carbon Dots; SOD, Superoxide Dismutase; STAT3, Signal Transducer and Activator of Transcription 3; TCM, Traditional Chinese Medicine; TCM-CDs, Traditional Chinese Medicine-derived Carbon Dots Nanozymes; TNF-α, Tumor Necrosis Factor-α; UC, Ulcerative colitis.

Availability of Data and Materials

For data requests, please contact the corresponding authors.

Author Contributions

Conceptualization: CYH, QL, MLC and MXZ; formal analysis and investigation: CYH, CXX, YFL and ZZ; funding acquisition and supervision: QL; writing—original draft preparation: CYH; writing—review and editing: MLC, MXZ. All authors have read and agreed to the published version of the manuscript.

Ethics Approval and Consent to Participate

Not applicable.

Acknowledgments

None.

Funding

This work was supported by the Innovation Team of Xi'an Medical University (2021TD15), Xi'an Science and Technology Program Project (2024JH-YLYB-0359, 2025JH-YXYJYB-0398), Special Service Project of Shaanxi Provincial Department of Education (24JC079), Supporting Fund Project of the First Affiliated Hospital of Xi'an Medical University (XYFYPT-2023-04, XYFYPT-2023-06,XYFYPT-RC-2024-02), Xi'an Weiyang District Project (202412).

Conflict of Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

[1] Torres J, Burisch J, Riddle M, Dubinsky M, Colombel JF. Preclinical disease and preventive strategies in IBD: perspectives, challenges and opportunities. Gut. 2016; 65: 1061–1069. https://doi.org/10.1136/gutjnl-2016-311785.

[2] Manski S, Noverati N, Policarpo T, Rubin E, Shivashankar R. Diet and nutrition in inflammatory bowel disease: a review of the literature. Crohn's & Colitis 360. 2024; 6: otad077. https://doi.org/10.1093/crocol/otad077.

[3] Kumar A, Smith PJ. Horizon scanning: new and future therapies in the management of inflammatory bowel disease. eGastroenterology. 2023; 1: e100012. https://doi.org/10.1136/egastro-2023-100012.

[4] Wu T, Bai X, Zhang Y, Dai E, Ma J, Yu C, *et al*. Natural medicines-derived carbon dots as novel oral antioxidant administration strategy for ulcerative colitis therapy. Journal of nanobiotechnology. 2024; 22: 511. https://doi.org/10.1186/s12951-024-02702-2.

[5] Chandio I, Ai Y, Wu L, Liang Q. Recent progress in MOFs-based nanozymes for biosensing. Nano Research. 2024; 17: 39–64. https://doi.org/10.1007/s12274-023-5770-3.

[6] Li X, Zhu H, Liu P, Wang M, Pan J, Qiu F, *et al*. Realizing selective detection with nanozymes: Strategies and trends. TrAC Trends in Analytical Chemistry. 2021; 143: 116379. https://doi.org/10.1016/j.trac.2021.116379.

[7] Lopez-Cantu DO, González-González RB, Melchor-Martínez EM, Martínez SAH, Araujo RG, Parra-Arroyo L, *et al*. Enzyme-mimicking capacities of carbon-dots nanozymes: Properties, catalytic mechanism, and applications–A review. International Journal of Biological Macromolecules. 2022; 194: 676–687. https://doi.org/10.1016/j.ijbiomac.2021.11.112.

[8] Sun Y, Xu B, Pan X, Wang H, Wu Q, Li S, *et al*. Carbon-based nanozymes: Design, catalytic mechanism, and bioapplication. Coordination Chemistry Reviews. 2023; 475: 214896. https://doi.org/10.1016/j.ccr.2022.214896.

[9] Jin J, Li L, Zhang L, Luan Z, Xin S, Song K. Progress in the application of carbon dots-based nanozymes. Frontiers in Chemistry. 2021; 9: 748044. https://doi.org/10.3389/fchem.2021.748044.

[10] Gao W, He J, Chen L, Meng X, Ma Y, Cheng L, *et al*. Deciphering the catalytic mechanism of superoxide dismutase activity of carbon dot nanozyme. Nature communications. 2023; 14: 160. https://doi.org/10.1038/s41467-023-35828-2.

[11] Shen Y, Zhang R, Wang Y. One-pot hydrothermal synthesis of metal-doped carbon dot nanozymes using protein cages as precursors. RSC advances. 2023; 13: 6760–6767. https://doi.org/10.1039/D2RA07222J.

[12] Gao W, Mu Y, Xiao L, Xiao Y. Designs, applications, and future perspectives of nanozymes in orthopedics and dentistry. European Cells and Materials. 2025; 52: 80–97. https://doi.org/10.22203/eCM.v052a06

[13] He Q, Zhang L. Design of carbon dots as nanozymes to mediate redox biological processes. Journal of Materials Chemistry B. 2023; 11: 5071–5082. https://doi.org/10.1039/d2tb02259a.

[14] Zheng K, Song R, Li R, Liu M, Ba Y, Jiang W, *et al*. Nanomaterials for refining tumor microenvironment and enhancing therapy in head and neck squamous cell carcinoma: a review. Oncology and Translational Medicine. 2024; 10: 151–161. https://doi.org/10.1097/ot9.0000000000000046.

[15] Ji C, Zhou Y, Leblanc RM, Peng Z. Recent developments of carbon dots in biosensing: A review. ACS sensors. 2020; 5: 2724–2741. https://doi.org/10.1021/acssensors.0c01556.

[16] Karthika V, Sridharan B, Nam JW, Kim D, Gyun Lim H. Neuromodulation by nanozymes and ultrasound during Alzheimer's disease management. Journal of nanobiotechnology. 2024; 22: 139. https://doi.org/10.1186/s12951-024-02406-7.

[17] Jacob E, Mathew D, Benny L, Varghese A. Emerging nanomaterials as versatile nanozymes: a new dimension in biomedical research. Topics in Current Chemistry (Cham). 2024; 382: 28. https://doi.org/10.1007/s41061-024-00473-w.

[18] Ansari MA, Shoaib S, Chauhan W, Gahtani RM, Hani U, Alomary MN, *et al*. Nanozymes and carbon-dots based nanoplatforms for cancer imaging, diagnosis and therapeutics: Current trends and challenges. Environmental Research. 2024; 241: 117522. https://doi.org/10.1016/j.envres.2023.117522.

[19] Jiang G, Fan J, Wan Y, Li J, Pi F. Enhanced photocatalytic and antimicrobial activities of carbon-dots nanozymes modulated with P-doping. Chemical Engineering Journal. 2024; 480: 148216. https://doi.org/10.1016/j.cej.2023.148216.

[20] Govindarasu M, George Joy J, Sharma G, Kim JC. Regulation of signaling pathways by metal and metal-doped nanozymes in inflammatory bowel disease: A therapeutic perspective. Nano Today. 2025; 63: 102747. https://doi.org/10.1016/j.nantod.2025.102747.

[21] Zhang J, Pang H, Tang H, Tu Q, Xia F, Zhang H, *et al*. The pharmacodynamic and pharmacological mechanisms underlying nanovesicles of natural products: Developments and challenges. Pharmacology & Therapeutics. 2025; 265: 108754. https://doi.org/10.1016/j.pharmthera.2024.108754.

[22] Qiu C, Zhang JZ, Wu B, Xu CC, Pang HH, Tu QC, *et al*. Advanced application of nanotechnology in active constituents of Traditional Chinese Medicines. Journal of nanobiotechnology. 2023; 21: 456. https://doi.org/10.1186/s12951-023-02165-x.

[23] Zhang J, Zou L, Li Q, Wu H, Sun Z, Xu X, *et al*. Carbon dots derived from traditional Chinese medicines with bioactivities: A rising star in clinical treatment. ACS Applied Bio Materials. 2023; 6: 3984–4001. https://doi.org/10.1021/acsabm.3c00462.

[24] Novoselov KS, Geim AK, Morozov SV, Jiang D, Zhang Y, Dubonos SV, *et al*. Electric field effect in atomically thin carbon films. Science. 2004; 306: 666–669. https://doi.org/10.1126/science.1102896.

[25] Danilov M, Fomanyuk S, Dovbeshko G, Gnatyuk O, Rusetskyi I, Kolbasov GY. Graphene quantum dots from partially unzipped multi-walled carbon nanotubes: promising materials for oxygen electrodes. Journal of The Electrochemical Society. 2021; 168: 044514. https://doi.org/10.1149/1945-7111/abf4b3.

[26] Mansuriya BD, Altintas Z. Applications of graphene quantum dots in biomedical sensors. Sensors (Basel, Switzerland). 2020; 20: 1072. https://doi.org/10.3390/s20041072.

[27] Ponomarenko LA, Schedin F, Katsnelson MI, Yang R, Hill EW, Novoselov KS, *et al*. Chaotic Dirac billiard in graphene quantum dots. Science. 2008; 320: 356–358. https://doi.org/10.1126/science.1154663.

[28] Chen LC, Xiao YK, Ke NJ, Shih CY, Yeh TF, Lee YL, *et al*. Synergy between quantum confinement and chemical functionality of graphene dots promotes photocatalytic H_2 evolution. Journal of Materials Chemistry A. 2018; 6: 18216–18224. https://doi.org/10.1039/C8TA05288C.

[29] Ritter KA, Lyding JW. The influence of edge structure on the electronic properties of graphene quantum dots and nanoribbons. Nature materials. 2009; 8: 235–242. https://doi.org/10.1038/nmat2378.

[30] Cayuela A, Soriano M, Carrillo-Carrión C, Valcárcel M. Semiconductor and carbon-based fluorescent nanodots: the need for consistency. Chemical communications (Cambridge, England). 2016; 52: 1311–1326. https://doi.org/10.1039/c5cc07754k.

[31] Liu Z, Zou H, Wang N, Yang T, Peng Z, Wang J, *et al*. Photoluminescence of carbon quantum dots: coarsely adjusted by quantum confinement effects and finely by surface trap states. Science China Chemistry. 2018; 61: 490–496. https://doi.org/10.1007/s11426-017-9172-0.

[32] Li S, Li L, Tu H, Zhang H, Silvester DS, Banks CE, *et al*. The development of carbon dots: From the perspective of materials chemistry. Materials Today. 2021; 51: 188–207. https://doi.org/10.1016/j.mattod.2021.07.028.

[33] Dong X, Li W, Chen X, Zhuo E, Zhai Z, Qi H, *et al*. Ethylenediamine Assisted Synthesis of o-Phenylenediamine-Based Red Emissive Carbon Quantum Dots: A Strategy to Improve the Fluorescence Quantum Yield. Advanced Optical Materials. 2025; 13: 2402173. https://doi.org/10.1002/adom.202402173.

[34] Siddique AB, Singh VP, Pramanick AK, Ray M. Amorphous carbon dot and chitosan based composites as fluorescent inks and luminescent films. Materials Chemistry and Physics. 2020; 249: 122984. https://doi.org/10.1016/j.matchemphys.2020.122984.

[35] Margraf JT, Strauss V, Guldi DM, Clark T. The electronic structure of amorphous carbon nanodots. The Journal of Physical Chemistry B. 2015; 119: 7258–7265. https://doi.org/10.1021/jp510620j.

[36] Banger A, Gautam S, Jadoun S, Jangid NK, Srivastava A, Pulidindi IN, *et al*. Synthetic methods and applications of carbon nanodots. Catalysts. 2023; 13: 858. https://doi.org/10.3390/catal13050858.

[37] Strauss V, Kahnt A, Zolnhofer EM, Meyer K, Maid H, Placht C, *et al*. Assigning electronic states in carbon nanodots. Advanced Functional Materials. 2016; 26: 7975–7985. https://doi.org/10.1002/adfm.201602325.

[38] Garg B, Bisht T. Carbon nanodots as peroxidase nanozymes for biosensing. Molecules (Basel, Switzerland). 2016; 21: 1653. https://doi.org/10.3390/molecules21121653.

[39] Sameer M, Arif Y, Aqil A, Nadaf A, Rafiya K, Hasan N, *et al*. Carbon nanodots as a remedial nanovesicles for drug delivery. European Polymer Journal. 2023; 200: 112515. https://doi.org/10.1016/j.eurpolymj.2023.112515.

[40] Liu J, Li R, Yang B. Carbon dots: a new type of carbon-based nanomaterial with wide applications. ACS Central Science. 2020; 6: 2179–2195. https://doi.org/10.1021/acscentsci.0c01306.

[41] Hu C, Li M, Qiu J, Sun YP. Design and fabrication of carbon dots for energy conversion and storage. Chemical Society Reviews. 2019; 48: 2315–2337. https://doi.org/10.1039/c8cs00750k.

[42] Xia C, Zhong J, Han X, Zhu S, Li Y, Liu H, *et al*. The formation mechanism of carbonized polymer dots: Crosslinking-induced nucleation and carbonization. Angewandte Chemie (International ed. in English). 2024; 63: e202410519. https://doi.org/10.1002/anie.202410519.

[43] Kang C, Tao S, Yang F, Yang B. Aggregation and luminescence in carbonized polymer dots. Aggregate. 2022; 3: e169. https://doi.org/10.1002/agt2.169.

[44] Xia C, Zhu S, Feng T, Yang M, Yang B. Evolution and synthesis of carbon dots: from carbon dots to carbonized polymer dots. Advanced science (Weinheim, Baden-Württemberg, Germany). 2019; 6: 1901316. https://doi.org/10.1002/advs.201901316.

[45] Chen J, Luo JB, Hu MY, Zhou J, Huang CZ, Liu H. Controlled synthesis of multicolor carbon dots assisted by machine learning. Advanced Functional Materials. 2023; 33: 2210095. https://doi.org/10.1002/adfm.202210095.

[46] Li W, Wang X, Lin J, Meng X, Wang L, Wang M, *et al*. Controllable and large-scale synthesis of carbon quantum dots for efficient solid-state optical devices. Nano Energy. 2024; 122: 109289. https://doi.org/10.1016/j.nanoen.2024.109289.

[47] Tu H, Liu H, Xu L, Luo Z, Li L, Tian Y, *et al*. Carbon dots from alcohol molecules: principles and the reaction mechanism. Chemical science. 2023; 14: 12194–12204. https://doi.org/10.1039/d3sc04606k.

[48] Xiong Y, Schneider J, Reckmeier CJ, Huang H, Kasák P, Rogach AL. Carbonization conditions influence the emission characteristics and the stability against photobleaching of nitrogen doped carbon dots. Nanoscale. 2017; 9: 11730–11738. https://doi.org/10.1039/c7nr03648e.

[49] Xu Y, Wang C, Zhuo H, Zhou D, Song Q. The function-oriented precursor selection for the preparation of carbon dots. Nano Research. 2023; 16: 11221–11249. https://doi.org/10.1007/s12274-023-5873-x.

[50] Ferreyra DD, Sartori DR, Riega SDE, Rodríguez HB, Gonzalez MC. Tuning the nitrogen content of carbon dots in carbon nitride nanoflakes. Carbon. 2020; 167: 230–243. https://doi.org/10.1016/j.carbon.2020.05.062.

[51] Iravani S, Varma RS. Green synthesis, biomedical and biotechnological applications of carbon and graphene quantum dots. A review. Environmental chemistry letters. 2020; 18: 703–727. https://doi.org/10.1007/s10311-020-00984-0.

[52] Sharma A, Das J. Small molecules derived carbon dots: synthesis and applications in sensing, catalysis, imaging, and biomedicine. Journal of nanobiotechnology. 2019; 17: 92. https://doi.org/10.1186/

s12951-019-0525-8.

[53] Shi W, Han Q, Wu J, Ji C, Zhou Y, Li S, *et al*. Synthesis mechanisms, structural models, and photothermal therapy applications of top-down carbon dots from carbon powder, graphite, graphene, and carbon nanotubes. International journal of molecular sciences. 2022; 23: 1456. https://doi.org/10.3390/ijms23031456.

[54] Qu JH, Wei Q, Sun DW. Carbon dots: Principles and their applications in food quality and safety detection. Critical reviews in food science and nutrition. 2018; 58: 2466–2475. https://doi.org/10.1080/10408398.2018.1437712.

[55] Wang FT, Wang LN, Xu J, Huang KJ, Wu X. Synthesis and modification of carbon dots for advanced biosensing application. The Analyst. 2021; 146: 4418–4435. https://doi.org/10.1039/d1an00466b.

[56] Bian Z, Wallum A, Mehmood A, Gomez E, Wang Z, Pandit S, *et al*. Properties of carbon dots versus small molecules from "bottom-up" synthesis. ACS nano. 2023; 17: 22788–22799. https://doi.org/10.1021/acsnano.3c07486.

[57] Choi Y, Choi Y, Kwon OH, Kim BS. Carbon dots: bottom-up syntheses, properties, and light-harvesting applications. Chemistry, an Asian journal. 2018; 13: 586–598. https://doi.org/10.1002/asia.201701736.

[58] Bian Z, Gomez E, Gruebele M, Levine BG, Link S, Mehmood A, *et al*. Bottom-up carbon dots: purification, single-particle dynamics, and electronic structure. Chemical science. 2025; 16: 4195–4212. https://doi.org/10.1039/d4sc05843g.

[59] Yang S, Li Y, Chen L, Wang H, Shang L, He P, *et al*. Fabrication of carbon-based quantum dots via a "bottom-up" approach: Topology, chirality, and free radical processes in "Building Blocks". Small (Weinheim an der Bergstrasse, Germany). 2023; 19: 2205957. https://doi.org/10.1002/smll.202205957.

[60] Wang C, Li J, Liu K, Li J, Zhang F, Ma X, *et al*. Donkey-Hide Gelatin-Derived Carbon Dots Activate Erythropoiesis and Eliminate Oxidative Stress for Aplastic Anemia Treatment. ACS nano. 2025; 19: 2922–2935. https://doi.org/10.1021/acsnano.4c16766.

[61] Huo Y, Xiu S, Meng L-Y, Quan B. Solvothermal synthesis and applications of micro/nano carbons: A review. Chemical Engineering Journal. 2023; 451: 138572. https://doi.org/10.1016/j.cej.2022.138572.

[62] Wang B, Yu J, Sui L, Zhu S, Tang Z, Yang B, *et al*. Rational design of multi-color-emissive carbon dots in a single reaction system by hydrothermal. Advanced Science. 2021; 8: 2001453. https://doi.org/10.1002/advs.202001453.

[63] Lee A, Yun S, Kang ES, Kim JW, Park JH, Choi JS. Effect of heteroatoms on the optical properties and enzymatic activity of N-doped carbon dots. RSC advances. 2021; 11: 18776–18782. https://doi.org/10.1039/d1ra03175a.

[64] Tajik S, Dourandish Z, Zhang K, Beitollahi H, Van Le Q, Jang HW, *et al*. Carbon and graphene quantum dots: a review on syntheses, characterization, biological and sensing applications for neurotransmitter determination. RSC advances. 2020; 10: 15406–15429. https://doi.org/10.1039/d0ra00799d.

[65] Fang Q, Dong Y, Chen Y, Lu CH, Chi Y, Yang HH, *et al*. Luminescence origin of carbon based dots obtained from citric acid and amino group-containing molecules. Carbon. 2017; 118: 319–326. https://doi.org/10.1016/j.carbon.2017.03.061.

[66] Wu X, Zhao B, Zhang J, Xu H, Xu K, Chen G. Photoluminescence and photodetecting properties of the hydrothermally synthesized nitrogen-doped carbon quantum dots. The Journal of Physical Chemistry C. 2019; 123: 25570–25578. https://doi.org/10.1021/acs.jpcc.9b06672.

[67] Luo H, Papaioannou N, Salvadori E, Roessler MM, Ploenes G, van Eck ER, *et al*. Manipulating the optical properties of carbon dots by fine-tuning their structural features. ChemSusChem. 2019; 12: 4432–4441. https://doi.org/10.1002/cssc.201901795.

[68] Huang J, Wang M, Jiang X, Liu Y, Ge Y, Zhang C. Bletilla striata carbon dots with alleviating effect of DSS-induced ulcerative colitis. Biochemical and Biophysical Research Communications. 2024; 695: 149358. https://doi.org/10.1016/j.bbrc.2023.149358.

[69] Cui L, Ren X, Sun M, Liu H, Xia L. Carbon dots: Synthesis, properties and applications. Nanomaterials (Basel, Switzerland). 2021; 11: 3419. https://doi.org/10.3390/nano11123419.

[70] Liu J, Zhang Y, Miao X, Li H, Tao C, Liu J, *et al*. Rapid synthesis of nitrogen-doped carbon dots by microwave method for sensitive detection of co (II) in water environment. Diamond and Related Materials. 2025; 151: 111830. https://doi.org/10.1016/j.diamond.2024.111830.

[71] Tang H, Tang Y, Xiao M, Zhu H, Guo M. Study on microwave synthesis mechanism of carbon dots based on NMR characterization. Colloids and Surfaces A: Physicochemical and Engineering Aspects. 2022; 651: 129564. https://doi.org/10.1016/j.colsurfa.2022.129564.

[72] Jiang L, Cai H, Zhou W, Li Z, Zhang L, Bi H. RNA-targeting carbon dots for live-cell imaging of granule dynamics. Advanced Materials. 2023; 35: 2210776. https://doi.org/10.1002/adma.202210776.

[73] Li J, Fu W, Zhang X, Zhang Q, Ma D, Wang Y, *et al*. Green preparation of ginger-derived carbon dots accelerates wound healing. Carbon. 2023; 208: 208–215. https://doi.org/10.1016/j.carbon.2023.03.039.

[74] Lin R, Cheng S, Tan M. Green synthesis of fluorescent carbon dots with antibacterial activity and their application in Atlantic mackerel (Scomber scombrus) storage. Food & Function. 2022; 13: 2098–2108. https://doi.org/10.1039/d1fo03426j.

[75] Venugopalan P, Vidya N. Green synthesis of mango ginger (Curcuma amada) derived fluorescent carbon dots—a potent label-free probe for hexavalent chromium sensing in water. Spectroscopy Letters. 2022; 55: 373–388. https://doi.org/10.1080/00387010.2022.2082483.

[76] Ma Ca, Yin C, Fan Y, Yang X, Zhou X. Highly efficient synthesis of N-doped carbon dots with excellent stability through pyrolysis method. Journal of Materials Science. 2019; 54: 9372–9384. https://doi.org/10.1007/s10853-019-03585-7.

[77] Chaudhary P, Maurya DK, Yadav S, Pandey A, Tripathi RK, Yadav BC. Ultrafast responsive humidity sensor based on roasted gram derived carbon quantum dots: experimental and theoretical study. Sensors and Actuators B: Chemical. 2021; 329: 129116. https://doi.org/10.1016/j.snb.2020.129116.

[78] Zhao XX, Tao SY, Yang B. The classification of carbon dots and the relationship between synthesis methods and properties. Chinese Journal of Chemistry. 2023; 41: 2206–2216. https://doi.org/10.1002/cjoc.202300062.

[79] Zhang Y, Zhao J, Zhao Y, Bai X, Chen Y, Liu Y, *et al*. The Rhei radix rhizoma-based carbon dots ameliorates dextran sodium sulphate-induced ulcerative colitis in mice. Artificial Cells, Nanomedicine, and Biotechnology. 2023; 51: 180–191. https://doi.org/10.1080/21691401.2023.2197947.

[80] Wang X, Zhang Y, Zhang M, Kong H, Wang S, Cheng J, *et al*. Novel carbon dots derived from puerariae lobatae radix and their anti-gout effects. Molecules (Basel, Switzerland). 2019; 24: 4152. https://doi.org/10.3390/molecules24224152.

[81] Zhu X, Fu Q, Jiang L, Zheng L. Iron oxide nanoparticles for diagnosing and treating degenerative orthopaedic diseases: A review. European Cells and Materials. 2024; 48: 45–65. https://doi.org/10.22203/eCM.v048a04.

[82] Liu H, Zhong X, Pan Q, Zhang Y, Deng W, Zou G, *et al*. A review of carbon dots in synthesis strategy. Coordination Chemistry Reviews. 2024; 498: 215468. https://doi.org/10.1016/j.ccr.2023.215468.

[83] Cui Y, Yang D, Li Q, Peng Z, Zhong Z, Song Y, *et al*. Cu, Zn, I-doped carbon dots with boosted triple antioxidant nanozyme activity for treatment of DSS-induced colitis. ACS Applied Materials & Interfaces. 2024; 16: 32619–32632. https://doi.org/10.1021/acsami.4c03627.

[84] Gao F, Liu J, Gong P, Yang Y, Jiang Y. Carbon dots as potential antioxidants for the scavenging of multi-reactive oxygen and ni-

trogen species. Chemical Engineering Journal. 2023; 462: 142338. https://doi.org/10.1016/j.cej.2023.142338.

[85] Nie R, Zhang J, Jia Q, Li Y, Tao W, Qin G, *et al*. Structurally oriented carbon dots as ROS nanomodulators for dynamic chronic inflammation and infection elimination. ACS nano. 2024; 18: 22055–22070. https://doi.org/10.1021/acsnano.4c05266.

[86] Zeng M, Wang Y, Liu M, Wei Y, Wen J, Zhang Y, *et al*. Potential efficacy of herbal medicine-derived carbon dots in the treatment of diseases: from mechanism to clinic. International Journal of Nanomedicine. 2024; 19: 4043–4044. https://doi.org/10.2147/IJN.S431061.

[87] Strober W, Fuss I, Mannon P. The fundamental basis of inflammatory bowel disease. The Journal of clinical investigation. 2007; 117: 514–521. https://doi.org/10.1172/JCI30587.

[88] Zhang G, Song D, Ma R, Li M, Liu B, He Z, *et al*. Artificial mucus layer formed in response to ROS for the oral treatment of inflammatory bowel disease. Science Advances. 2024; 10: eado8222. https://doi.org/10.1126/sciadv.ado8222.

[89] Chen SS, Song BB, Gong XQ, Zhao J, Zhang KQ, Wang Q. Effects of tanshinone IIA on TNBS-induced mouse model of chronic colitis through PXR/NF-κB signaling pathway. Chinese Traditional Patent Medicine. 2025; 47: 1129-1136. https://doi.org/10.3969/j.issn.1001-1528.2025.04.010. (In Chinese)

[90] Zhu L, Gu P, Shen H. Protective effects of berberine hydrochloride on DSS-induced ulcerative colitis in rats. International Immunopharmacology. 2019; 68: 242–251. https://doi.org/10.1016/j.intimp.2018.12.036.

[91] Deng Z, Zhang Y, Li R, Zhu Y, Xu C, Gao B, *et al*. Honeysuckle-derived carbon dots with robust catalytic and pharmacological activities for mitigating lung inflammation by inhibition of caspase11/GSDMD-dependent pyroptosis. Advanced Functional Materials. 2025; 35: 2418683. https://doi.org/10.1002/adfm.202418683.

[92] Pal T, Mohiyuddin S, Packirisamy G. Facile and green synthesis of multicolor fluorescence carbon dots from curcumin: in vitro and in vivo bioimaging and other applications. ACS omega. 2018; 3: 831–843. https://doi.org/10.1021/acsomega.7b01323.

[93] Hanai H, Sugimoto K. Curcumin has bright prospects for the treatment of inflammatory bowel disease. Current pharmaceutical design. 2009; 15: 2087–2094. https://doi.org/10.2174/138161209788489177.

[94] Karthikeyan A, Young KN, Moniruzzaman M, Beyene AM, Do K, Kalaiselvi S, *et al*. Curcumin and its modified formulations on inflammatory bowel disease (IBD): The story so far and future outlook. Pharmaceutics. 2021; 13: 484. https://doi.org/10.3390/pharmaceutics13040484.

[95] Qiu C, Guo P, Wang C, Tu Q, Zhong L, Fu Y, *et al*. Synergistic gambogic acid/Ga^{3+} remodels the immunosuppressive tumor microenvironment to enhance triple-negative breast cancer therapy. Journal of nanobiotechnology. 2025; 23: 710. https://doi.org/10.1186/s12951-025-03758-4.

[96] Patel PJ, Gupte S, Naik R, Kailasa SK, Jha S, Patel SB, *et al*. Fruit peel derived carbon dots for improved curcumin delivery: a promising strategy for enhanced antimicrobial and antioxidant activity. ChemistrySelect. 2024; 9: e202400762. https://doi.org/10.1002/slct.202400762.

[97] Architha N, Ragupathi M, Shobana C, Selvankumar T, Kumar P, Lee YS, *et al*. Microwave-assisted green synthesis of fluorescent carbon quantum dots from Mexican Mint extract for Fe^{3+} detection and bioimaging applications. Environmental Research. 2021; 199: 111263. https://doi.org/10.1016/j.envres.2021.111263.

[98] Kong H, Zhao Y, Zhu Y, Xiong W, Luo J, Cheng J, *et al*. Carbon dots from Artemisiae Argyi Folium Carbonisata: strengthening the antifrostbite ability. Artificial Cells, Nanomedicine, and Biotechnology. 2021; 49: 11–19. https://doi.org/10.1080/21691401.2020.1862134.

[99] Cheng C, Zhao S, Cheng Y, Liu Y, Wei H. Design of nanozymes for inflammatory bowel disease therapy. Science China Life Sciences. 2021; 64: 1368-1371. https://doi.org/10.1007/s11427-020-1937-6.

[100] Yang L, Dai F, Tang H, Li M, An Y, Tan Y, *et al*. Lophatherum-Gracile driven near-infrared carbon dots inhibit ferroptosis and mitophagy to treat acute kidney injury. Chemical Engineering Journal. 2025; 513: 162637. https://doi.org/10.1016/j.cej.2025.162637.

[101] Long J, Liang X, Ao Z, Tang X, Li C, Yan K, *et al*. Stimulus-responsive drug delivery nanoplatforms for inflammatory bowel disease therapy. Acta Biomaterialia. 2024; 188: 27–47. https://doi.org/10.1016/j.actbio.2024.09.007.

[102] Cui M, Zhang M, Liu K. Colon-targeted drug delivery of polysaccharide-based nanocarriers for synergistic treatment of inflammatory bowel disease: A review. Carbohydrate Polymers. 2021; 272: 118530. https://doi.org/10.1016/j.carbpol.2021.118530.

[103] Leong CR, Tong WY, Tan W-N, Tumin ND, Yusof FAM, Yacob LS, *et al*. Synthesis of curcumin quantum dots and their antimicrobial activity on necrotizing fasciitis causing bacteria. Materials Today: Proceedings. 2020; 31: 31–35. https://doi.org/10.1016/j.matpr.2020.01.082.

[104] Rai M, Ingle AP, Törős G, Prokisch J. Assessing the efficacy of carbon nanodots derived from curcumin on infectious diseases. Expert Review of Anti-infective Therapy. 2024; 22: 1107–1121. https://doi.org/10.1080/14787210.2024.2409401.

[105] Mou Y, Bai X, Ma H, Li T, Zhao Y, Wu T, *et al*. Protective effect of carbon dots derived from scrambled Coptidis Rhizoma against ulcerative colitis in mice. Frontiers in Molecular Biosciences. 2023; 10: 1253195. https://doi.org/10.3389/fmolb.2023.1253195.

[106] Hu J, Luo J, Zhang M, Wu J, Zhang Y, Kong H, *et al*. Protective effects of radix sophorae flavescentis carbonisata-based carbon dots against ethanol-induced acute gastric ulcer in rats: anti-inflammatory and antioxidant activities. International Journal of Nanomedicine. 2021; 16: 2461–2475. https://doi.org/10.2147/IJN.S289515.

[107] Wu L, Xi Y, Yan M, Sun C, Tan J, He J, *et al*. Berberine-based carbon quantum dots improve intestinal barrier injury and alleviate oxidative stress in C57BL/6 mice with 5-fluorouracil-induced intestinal mucositis by enhancing gut-derived short-chain fatty acids contents. Molecules (Basel, Switzerland). 2023; 28: 2148. https://doi.org/10.3390/molecules28052148.

[108] Jiang J, Pan Z, Su Y, Dai L, Xu N, Wu H, *et al*. Carbon dots from purple sweet potato as a promising anti-inflammatory biomaterial for alleviating the LPS-induced inflammation in macrophages. Journal of nanobiotechnology. 2025; 23: 397. https://doi.org/10.1186/s12951-025-03494-9.

[109] Wang X, Wang X, Cao Y, Wang W, Liu D, Zhang J, *et al*. Nanoplatforms in sepsis storm: Multimodal synergy for precision immunomodulation and pathogen neutralizations. Pharmaceutical Science Advances. 2025; 3: 100087. https://doi.org/10.1016/j.psci a.2025.100087.

[110] Kan L, Zheng Z, Fu W, Ma Y, Wang W, Qian H, *et al*. Recent progress on engineered micro/nanomaterials mediated modulation of gut microbiota for treating inflammatory bowel disease. Journal of controlled release: official journal of the Controlled Release Society. 2024; 370: 43–65. https://doi.org/10.1016/j.jconrel.2024.04.014.

[111] Chen X, Luo X, Xiao M, Chen X, Wu L, You Y, *et al*. Oral Carbon Dots Derived from Cimicifugae rhizome Carbonization Products to Ameliorate Ulcerative Colitis. ACS applied materials & interfaces. 2025; 17: 57989–58000. https://doi.org/10.1021/acsami.5c14857.

[112] Yang M, Deng Z, Zhu Y, Xu C, Ding C, Zhang Y, *et al*. Advancements in herbal medicine-based nanozymes for biomedical applications. Chinese Medical Journal. 2025; 138: 1037–1049. https://doi.org/10.1097/CM9.0000000000003584.

[113] Huang Z, Wang J, Li C, Zheng W, He J, Wu Z, *et al*. Application of natural antioxidants from traditional Chinese medicine in the treatment of spinal cord injury. Frontiers in Pharmacology. 2022; 13: 976757. https://doi.org/10.3389/fphar.2022.976757.

[114] Lei F, Huang Q, Zhang C, Lin Y, Zhang Y, Wang F. Pathogenesis guided Application of Nanozymes in the Treatment of Inflammatory Bowel Disease. Materials Today Bio. 2025; 33: 102008. https://doi.org/10.1016/j.mtbio.2025.102008.

[115] Gaytan SL, Beaven E, Gadad SS, Nurunnabi M. Progress and prospect of nanotechnology for cardiac fibrosis treatment. Interdisciplinary Medicine. 2023; 1: e20230018. https://doi.org/10.1002/INMD.20230018.

[116] Xu C, Huang X, Deng Z, Wang R, Ghazimirsaeid S, Yao L, *et al*. Dendrobium Officinale-Derived Carbon Dots Nanozymes Alleviate Colitis by Orchestrating Intestinal Mucus-Epithelium-Immune Barriers. Advanced science (Weinheim, Baden-Württemberg, Germany). 2025; 12: e12567. https://doi.org/10.1002/advs.202512567.

[117] Li Y, Li Q, Zhu Y, Huang C, Li H, Deng Z, *et al*. Medicinal Plant-Derived Carbon Dots Nanozymes Ameliorate Ulcerative Colitis via Anti-inflammatory, Antioxidant, and Gut Barrier-Protective Effects. ACS Applied Materials & Interfaces. 2025; 17: 42751–42766. https://doi.org/10.1021/acsami.5c08068.

[118] Guo Y, Yang L, Yao L, Zhou C, Zhu Y, Xu C, *et al*. Carbon dots derived from Ligusticum Chuanxiong mitigate cardiac injury by disrupting the harmful oxidative stress-apoptosis cycle. Journal of nanobiotechnology. 2025; 23: 391. https://doi.org/10.1186/s12951-025-03477-w.

[119] Gubatan J, Levitte S, Patel A, Balabanis T, Wei MT, Sinha SR. Artificial intelligence applications in inflammatory bowel disease: emerging technologies and future directions. World journal of gastroenterology. 2021; 27: 1920–1935. https://doi.org/10.3748/wjg.v27.i17.1920.

[120] Mian SM, Khan MS, Shawez M, Kaur A. Artificial intelligence (AI), machine learning (ML) & deep learning (DL): A comprehensive overview on techniques, applications and research directions. 2024 2nd International Conference on Sustainable Computing and Smart Systems (ICSCSS). 2024; 1404–1409. https://doi.org/10.1109/ICSCSS60660.2024.10625198.

[121] Sacks D, Baxter B, Campbell BCV, Carpenter JS, Cognard C, Dippel D, *et al*. Multisociety Consensus Quality Improvement Revised Consensus Statement for Endovascular Therapy of Acute Ischemic Stroke. International Journal of Stroke. 2018; 13: 612–632. https://doi.org/10.1177/1747493018778713.

[122] Liu T, Chen L, Zhao X, Xie M, Xie L, Wang M, *et al*. An AI-assisted designed supramolecularly engineered nanoplatform reverses pigmentation by triggering an ineffective compensatory melanin production program. Bioactive materials. 2026; 60: 243–260. https://doi.org/10.1016/j.bioactmat.2026.01.027.

[123] Zhang A, Sun Y, Zhang S, Feng Y, Ding K, Luo T. From Ambiguity to Precision: Carbon Dots Bridge Traditional Charcoal Medicine and Modern Nanomedicine. BIOI. 2026; 7. https://doi.org/10.15212/bioi-2025-0212.

[124] Iacucci M, Maeda Y, Santacroce G, Ghosh S. AI-enabled 'endo-histo-omics': breaking down intestinal barriers in IBD. Nature Reviews Gastroenterology & Hepatology. 2025; 22: 362–363. https://doi.org/10.1038/s41575-025-01051-1.

[125] Little RD, Jayawardana T, Koentgen S, Zhang F, Connor SJ, Boussioutas A, *et al*. Pathogenesis and precision medicine for predicting response in inflammatory bowel disease: advances and future directions. eGastroenterology. 2024; 2: e100006. https://doi.org/10.1136/egastro-2023-100006.

[126] Zhang DD, Wang PY. Intestinal stem cells (ISCs): ISCs-derived organoids for disease modeling and therapy. European Cells and Materials. 2025; 50: 84–86. https://doi.org/10.22203/eCM.v050a05.

Editor's note: The Scientific Editors responsible for this paper were Yang Liu and Kelong Fan.

Received: 26th December 2025; **Accepted**: 18th May 2026; **Published**: 31st August 2026