Review Article

Green Synthesis of Cobalt Ferrite Nanoparticles: An Emerging Material for Environmental and Biomedical Applications

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Research and utilization of nanotechnology are growing exponentially in every aspect of life. The constant growth of applications for magnetic nanoparticles, specifically nanoferrites, attracted many researchers. Among them, nanocobalt ferrite is the most crucial and studied magnetic nanoparticle. Environmentally benign synthetic methods became necessary to minimize environmental and occupational hazards. Green synthesis approaches in science and technology are now widely applied in the synthesis of nanomaterials. Herein, we reviewed recent advances in synthesizing nanocobalt ferrites and their composites using various scientific search engines. Subsequently, various applications were discussed, such as environmental (treatment of water/wastewater, photocatalytic degradation of dyes, and nanosorbent for environmental remediation) and biomedical (nanobiosensors for cancer diagnosis at the primary stage, effective targeted drug delivery, magnetic resonance imaging, hyperthermia, and potential drug candidates against cancer and microbial infections). This review offers comprehensive knowledge on how to choose appropriate natural resources for the green synthesis of nanocobalt ferrite and the benefits of this approach compared to conventional methods.

1. Introduction

Nanomaterial research is understanding and utilizing unique morphological and physicochemical properties of the large surface area of small particles (average size of 1–100 nm) for diverse applications in almost all fields of science and technology [1, 2]. It is one of the most favorite research area in chemistry, physics, biology, material science, medicine, pharmacy, and engineering [3]. Moreover, it is a single platform that connects these fields as multidisciplinary. MFe2O4 is the chemical formula of ferrite spinels, where M denotes divalent metal cations like cobalt, zinc, copper, nickel, manganese, etc. Nanoferrites are among the magnetic nanoparticles that possess many useful properties such as magnetic, electrical, gas sensing, energy storage devices, catalyst in organic reaction transformations, and biomedical (antibacterial, anticancer, MRI agents, etc.) across various technological and industrial applications [4].

The important factor that affects crystallinity, surface area, and chemical and physical properties is basically depends on the synthesis methods. Precise crystal structure and composition are essential for these properties. These properties depend on the size of particles, the ratio of surface area to volume, texture of crystallography, arrangement of elements, type of cations and position in the crystal lattice, impurities concentrations in traces, and the shape of the grain [5]. Various conventional methods are available for the synthesis of nanomaterials with the desired characteristics [6], as shown in Figure 1. However, these synthetic methodologies are neither eco-friendly nor economical and undergo sintering, pH, surfactants, solvents,
organic salts, etc. Therefore, these methods have multiple disadvantages and are difficult for large-scale synthesis [2].

Cobalt ferrite (CoFe$_2$O$_4$) nanoparticles and their composites are one of the most crucial and studied classes of magnetic nanoparticles. It has special chemical/physical/mechanical properties such as it exhibits various redox states, excellent permeability, superior electrochemical stability, excellent chemical stability, mechanical hardness, wear resistance, ease of synthesis, electrical insulation, high Curie temperature, high coercivity, moderate saturation magnetization, high anisotropy constant, and high magnetostriuctive are some unique features. These exceptional properties offer diverse applications in various fields [7, 8]. Magnetic nanoparticles can be characterized by various analytic tools reported in the literature such as ultraviolet (UV) spectroscopy, Fourier transform infrared (FTIR) spectroscopy, transmission electron microscopy (TEM), scanning electron microscopy (SEM), atomic force microscopy (AFM), dynamic light scattering (DLS), X-ray photoelectron spectroscopy (XPS), X-ray diffraction (XRD), single-phase inductively coupled plasma mass spectrometry (ICPMS), X-ray fluorescence (XRF) spectroscopy, auger electron spectroscopy (AES), X-ray absorption fine structure (XAFS), magnetic nanoparticles coupled high-performance liquid chromatography (HPLC), energy dispersive X-ray (EDX) analysis, and Raman spectroscopy, as shown in Figure 2. The rapid increase in publications in recent years indicates popularity among researchers across the nanotechnology field.

Now researchers are keen to reduce the toxic effects of chemicals on the environment by developing new methods and techniques [9]. Hence, one of the most focused areas of nanomaterial synthesis is utilizing natural resources like plants, products obtained from plants, and microorganisms (bacteria, fungi, yeast, algae, etc.) [10]. At the initial stage of chemical processes, green chemistry researchers utilize chemicals that minimize environmental risks and prevent pollution. Magnetic nanoparticles obtained from green synthesis exhibit little toxicity and elevated biocompatibility, which grant their biomedical utilization, typically for targeted drug delivery, contrast imaging, magnetic hyperthermia, anticancer, antimicrobial, etc. [11, 12].

2. Green Synthesis of Nanocobalt Ferrite

Recently, the utilization of green synthesis has captured attention in various fields. The amalgamation of nanosynthesis and green chemistry has vast potential for advancing novel
and vital nanoferrites that improve human health, protect the environment, and benefit industries. There are many reports available on the green synthesis of nanoferrites but their count is significantly less compared with conventional synthesis techniques. A recent comprehensive review reported that the number of research articles on nanoferrite commenced rising exponentially in the last couple of decades. Most significantly, the publications on cobalt ferrite exceeded other ferrites by far. The authors concluded by searching in the Web of Science Core Collection with the keyword “M ferrite” (where M = metals like cobalt, copper, nickel, manganese, and zinc); cobalt ferrite leading the chart, zinc ferrite as runner-up, followed by nickel ferrite, manganese ferrite, and copper ferrite [13]. Figure 3 shows different green precursors utilized in the synthesis of nanocobalt ferrite. The biosynthesis of nanomaterial was derived from living organisms like plants and microorganisms [14]. Green synthesis is more advantageous than traditional chemical synthesis since it most economical, reduces pollution, and enhances environmental and human health safety. However, because of present environmental complications and pollution associated with chemical synthesis, green synthesis provides alternate progress prospects and possible diverse applications [15].

Numerous organic (ascorbic acid, amino acids, starch, glucose, and gluconic acid) and inorganic components present in the plant extract act like reducing and stabilizing agents (to suppress aggregations). The activity of nitrate reductase, shuttle electrons quinones, and mixed mechanisms was proposed [16]. These biosynthesis approaches are widely accepted and selected for their eco-friendly, economical, sustainability, reproducibility, and excellent yield [17]. Ferromagnetic cobalt ferrite was synthesized using convective heating (in a hot air oven at 180°C for 3 hr) and microwave heating methods (at a frequency of 2.54 GHz at 850 W output power for 15 min) to afford 300–500 and 5–55 nm average crystallite size, respectively. Co(NO₃)₂·6H₂O and Fe(NO₃)₃·9H₂O are used as precursors because of their higher solubility and ability to form a homogeneous mixture using okra (Abelmoschus esculentus) plant extract as a reducing agent. Microwave heating methods exhibit excellent structural, optical, and magnetic properties than conventional heating methods. The smaller size particles via microwave heating methods were prone to interact quickly with the bacteria and disrupt the cell membrane effectively. This process leads to cell death. The antibacterial activity was performed on Gram-negative (Enterobacter aerogenes and Yersinia enterocolitica) and Gram-positive (Staphylococcus aureus and Micrococcus luteus) bacterial strains. Aspergillus aureus (AN) and Candida kru sei (CK) strains were utilized for antifungal activity. The inhibition zone confirms the biocidal activity. The results showed that the inhibiting zones are directly proportional to the concentration. The highest inhibition zone was observed against Y. enterocolitica (16 mm) in bacteria and C. kru sei (15 mm) in fungi, respectively, and offers new avenues in the treatment of various infections [18]. Moreover, okra plant extract also furnishes Ag-substituted CoFe₂O₄ [19].

Five research groups used honey for the green synthesis of nanocomposites of cobalt ferrite. Honey, as a stabilizer and reducing agent, has several advantages. Additionally, many carbohydrates and vitamins are vital constituents of honey, which are mild reducing agents and are subsequently responsible for controlled nanoparticle size. Agglomeration of nanoparticles can be prevented by stabilizing with proteins: (a) the honey-mediated synthesis of superparamagnetic cobalt–zinc ferrites nanoparticles with crystallite size around 14 ± 2 nm can easily remove Pb²⁺ (dangerous environmental pollutant) from water through adsorption capacity of 23.10 mg/g (for Co₀.₈Zn₀.₂Fe₂O₄) by Langmuir, Freundlich, and Dubinin–Radushkevich models. Co₀.₄Zn₀.₆Fe₂O₄ exhibits higher specific loss power (2.56 W/g) and the intrinsic loss power (0.40 nH·m²·kg⁻¹) coefficients at a magnetic field of 100 Oe with the frequency of 100 kHz compared to commercial Fe₃O₄. Hence, it can be successfully utilized in magnetic hyperthermal therapy [20]; (b) magnetic CoFe₂O₄ and CoFe₂O₄/g-C₃N₄ nanocomposite were prepared using honey by green synthesis, and photocatalytic activity was investigated by degradation of methylene blue (MB). Furthermore, the environmental remediation was achieved by the removal of the toxic lead (Pb²⁺) metal from the water [21]; (c) magnetic CoFe₂−xAlₓO₄ nanocrystals, prepared by simple sol–gel autoignition method using honey (glucose/fructose)
(d) Ag-substituted nanocobalt ferrites were furnished by combustion method with the assistance of honey with 24–41 nm size. Antibiotic susceptibility studies were carried out against *S. aureus* (ATCC 25923), *Escherichia coli* (ATCC 25922), and *Candida albicans* (ATCC 10231) using agar well diffusion method on Mueller–Hinton agar plates. Both nanomaterials exhibit zone of inhibition >7 mm for 100 mg and 10–20 mm for 500 mg concentration against positive control (streptomycin: 18–29 mm for 10 mg). Hence, Ag-doped CoFe₂O₄ was effective antimicrobial agents [23]; (e) structural, magnetic, and bandgap properties of chromium-substituted cobalt ferrite, prepared using honey, were evaluated [24].

*Hibiscus rosa-sinensis*, a medicinal herb, consists of various chemical compositions like organic and phenolic acids (citric, malic, succinic, lactic, gallic, hibiscus, and homogenitic acids) and flavonoids (quercetin, luteolin, gossypetin, and their glycosides) that exhibit excellent chelating/gelling agent. Two reports were available using *Hibiscus* flower and leaf extracts: (a) the cobalt ferrite (CoFe₂O₄) and silver–cobalt

![Figure 3: Green precursor utilized in synthesis and application of nanocobalt ferrite.](image-url)
ferrite (Ag–CoFe₂O₄) were synthesized by self-combustion process and wet ferritization reaction with 10–18 and 18.8 nm crystallite size, respectively. The antimicrobial activity was assayed on Gram-negative (E. coli ATCC 8739 and Pseudomonas aeruginosa ATCC 27853) and Gram-positive (S. aureus ATCC 6538, Enterococcus faecalis ATCC 29212, Staphylococcus saprophyticus ATCC 15305, and Bacillus subtilis ATCC 6633) bacterial strains and C. albicans ATCC 26790 as fungal strains. Incorporation of silver improved antimicrobial activity as compared to solo CoFe₂O₄ nanoparticles, exhibiting very low minimum inhibitory concentration (MIC) values ranging from 0.031 to 0.062 mg/mL against all tested microbial strains [25] and (b) cobalt ferrite obtained by chemical coprecipitation method as room temperature-based humidity sensors was also reported [26]. Phenylpropanoid, zingerone, gingerol, oxalic acid, ascorbic acid, and shogaol are the main chemical components of ginger (Zingiber officinale), whereas cardamom (Elettaria cardamomum) seeds consist of gallic acid, ferulic acid, isofuric acid, chlorogenic acid, caffeic acid, luteolin, quercetin, rutin, etc. This chemical composition, a combination of biomolecules, acts as capping agents, reducing/stabilizing and chelating agents, and even as fuel, eventually establishing aqueous ginger/cardamom extracts as a promising green sources for the synthesis of nanomaterials. The crystalline cobalt ferrite with an average crystallite size of 100 nm was successfully synthesized using iron nitrate/cobalt nitrate with aqueous extracts of ginger/cardamom through self-combustion method [27]. The ferromagnetic cobalt ferrite nanoparticles were synthesized using starch from the stem of sago palm (Metroxylon sagu) by the sol–gel synthesis with a particle size of 30–500 nm. The magnetization and coercive field of nanoparticles are inversely proportional to the increased amount of sago gel used during synthesis [28]. Polyphenols (quercetin) and phenol carboxylic acid (gallic acid), present in the ethanol extracts of Artemisia annua L. "hairy" roots, are primarily responsible for the synthesis of relatively stable nano-Ce₂O₃ without aggregation for at least 6 months. The extracts of "hairy" root samples showed higher reducing activity (the ability to reduce ferric Fe³⁺ ions of extracts) than the control samples. These nanoferrites inhibit substantially roots growth. The environmental remediation by eliminating metal ions such as Cu(II), Co(II), Ni(II), and Cd(II) from natural river water with the experimental recovery in the range of 86%–106% by adequate adsorption capacity was also reported [29].

The aromatic hydroxyl group in polyphenolic acid (secondary metabolite in rambutan peel extract (Nephelium lappaceum L.)) is responsible as a capping agent to afford regular and homogeneous nanomaterials. The phenolic hydroxyl groups of polyphenols bind effectively with the metal to furnish a metal phenolate complex by the chelating effect. Such complex subsequently resulted in superparamagnetic ZnO/CoFe₂O₄ nanorod by heat treatment. The composite ZnO/CoFe₂O₄ possesses a small bandgap, which displays light absorption capacity. The amalgamation of an n-type semiconductor (ZnO) and a p-type semiconductor (CoFe₂O₄) furnished homogeneous fine particles grains with conducive bandgap to exhibit excellent photocatalytic activity with 99.6% degradation of Direct Red 81 dye by solar light after 2 hr [30]. CoFe₂O₄ and Ag₃Co₁₋ₓFe₂O₄ were synthesized with eco-friendly green method via sol–gel autocombustion method with extracts from tulsi seed (Ocimum sanctum) and garlic cloves (Allium sativum). The antibacterial activity of synthesized nanomaterials was tested on E. coli and Listeria monocytogenes strains by disk diffusion method. The average zone of inhibition for both strains is 7–9 mm. Moreover, dopant (Ag concentration) has positive impact on antibacterial activity that increases by inducing the higher surface oxygen species, subsequently killing the bacteria [31]. Two researchers developed efficient conventional sol–gel autocombustion [32] and microwave combustion [33] methods using aloe vera plant extract for the preparation of CoFe₂O₄ nanostructures. The comprehensive summary of recently reported (2015–2021) green synthesis of cobalt ferrite with various green agents is given in Table 1.

A simple method is reported by the “green” route using grape peel extract and grape pulp extract to get cobalt ferrite nanoparticles with ~5 and ~25 nm crystallite sizes, respectively. These nanoparticles were found to be active in the decomposition of hydrogen peroxide [34]. Grape juice, as a novel and green fuel, is used to prepare nano-CoFe₂O₄@SiO₂@Dy₂CoO₄ nanocomposite as recyclable photocatalyst [35]. The aqueous extracts of sesame (Sesamum indicum L.) seeds were successfully used to prepare the nanocobalt ferrites through self-combustion and wet ferritization methods with sizes between 3 and 20 nm. The antimicrobial activity was evaluated on Gram-negative (E. coli ATCC 8739, P. aeruginosa ATCC 27853) and Gram-positive (S. aureus ATCC 6538, E. faecalis ATCC 29212) bacterial and fungal (C. albicans ATCC 10231) strains. Synthesized nanoparticles exhibited lower MIC values against E. faecalis (0.25–0.5 mg/mL), P. aeruginosa (0.125 mg/mL), and C. albicans (>1 mg/mL), whereas the antibiofilm activity was manifested at both high and low concentrations. All tested ferrites found to be non-cytotoxic at lower concentrations (7.8–250 mg/mL), whereas at higher concentrations (500–1,000 mg/mL) exhibited high toxicity on the human ileocecal colorectal adenocarcinoma (HCT-8) cell line [36]. CoFe₂O₄@ZnO–CeO₂ magnetic nanocomposite was prepared by eco-friendly and economical process with Crataegus microphylla fruit extract with 70–80 nm size. The antibacterial effect was investigated against E. coli, P. aeruginosa, and S. aureus strains. However, only S. aureus showed excellent antibacterial activity. The photocatalytic performance was examined by degradation of humic acid (HA). After 100 min, 97.2% and 72.4% of HA pollutants were degraded successfully under exposure of UV and visible light irradiations, respectively [37].

A highly stable and dispersed composite of cobalt ferrite–silica was prepared using an herbal material (Salix alba bark extract) via the self-propagating sol–gel process to furnish 15 nm particle size. The saturation magnetization values were found to be directly proportional to the amount of S. alba bark extract used for synthesis. The adsorption equilibrium of Malachite green (MG) (triphenyl methane dye) onto CoFe₂O₄/SiO₂ possesses monolayer adsorption with a capacity of 75.5 ± 1.21 mg g⁻¹, demonstrated by the
<table>
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<th>Sr. No.</th>
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<th>Method used</th>
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<th>Size (nm)</th>
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Table 1: Continued.

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<td>7</td>
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<td>36</td>
<td>Lemon juice</td>
<td>Sol–gel autocombustion</td>
<td>CoFe₁₉Sm₀₁O₄</td>
<td>10–22</td>
<td>NA</td>
<td>[48]</td>
</tr>
<tr>
<td>37</td>
<td>Sucrose/lemon juice</td>
<td>Modified Pechini method</td>
<td>CoFe₂O₄</td>
<td>NA</td>
<td>Anticancer drug (doxorubicin) delivery</td>
<td>[49]</td>
</tr>
<tr>
<td>38</td>
<td>Plant (cardamom seeds, date fruits, flaxseed, tragacanth gum, lavender seeds, and moringa) extract</td>
<td>Sol–gel</td>
<td>Co₉₃Ni₀₃Nd₀₂O₁₉Fe₁₈O₄</td>
<td>NA</td>
<td>Antimicrobial activity against <em>S. aureus</em> strain; anticancer activity on HeLa and HCT-116 cell lines</td>
<td>[50]</td>
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<td>Sr. No.</td>
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<td>Method used</td>
<td>Nanomaterial obtained</td>
<td>Size (nm)</td>
<td>Applications</td>
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<td>40</td>
<td>Fungus <em>Monascus purpureus</em> ATCC16436 cell-free culture filtrate</td>
<td>NA</td>
<td>CoFe$_2$O$_4$</td>
<td>NA</td>
<td>Antioxidant; anticancer activity on MCF-7, HepG2, and HFB-4 cell lines; antimicrobial activity against <em>S. aureus</em>, <em>E. coli</em>, <em>K. pneumoniae</em>, <em>P. aeruginosa</em>, <em>A. niger</em>, <em>A. solani</em>, <em>F. oxysporum</em>, and <em>C. albicans</em> strains</td>
<td>[51]</td>
</tr>
<tr>
<td>41</td>
<td>Egg white</td>
<td>Autocombustion Sol–gel self-propagation</td>
<td>CoFe$_2$O$_4$</td>
<td>42</td>
<td>NA</td>
<td></td>
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<td>42</td>
<td>Sol–gel self-propagation</td>
<td>Na</td>
<td>CoFe$_2$O$_4$</td>
<td>28–50</td>
<td>Biocompatibility (cytotoxicity, cell viability)</td>
<td>[53]</td>
</tr>
<tr>
<td>43</td>
<td>Egg white</td>
<td>Na</td>
<td>CoFe$_2$O$_4$</td>
<td>45</td>
<td>Remove anionic brilliant blue-R (BB-R) dye from the aqueous phase</td>
<td>[54]</td>
</tr>
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<td>44</td>
<td>E. coli</td>
<td>NA</td>
<td>CoFe$_2$O$_4$</td>
<td>3.6–5.5</td>
<td>Photodegradation of methylene blue in the presence of H$_2$O$_2$ under visible light</td>
<td>[55]</td>
</tr>
<tr>
<td>45</td>
<td>Sol–gel route</td>
<td>Wet chemical process</td>
<td>CoFe$_2$O$_4$</td>
<td>13–43</td>
<td>Photocatalytic; antibacterial activity against <em>S. aureus</em>, <em>E. faecalis</em>, <em>P. aeruginosa</em>, and <em>S. typhi</em> strains</td>
<td>[56]</td>
</tr>
<tr>
<td>46</td>
<td>Andrographis paniculata (Acanthaceae) plant extract</td>
<td>Microwaves-assisted method</td>
<td>NiCoFe$_2$O$_4$</td>
<td>26</td>
<td>Photocatalytic; antibacterial activity against <em>S. aureus</em>, <em>E. faecalis</em>, <em>P. aeruginosa</em>, and <em>S. typhi</em> strains</td>
<td>[57]</td>
</tr>
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<td>47</td>
<td>Cydonia oblonga extract</td>
<td>Coprecipitation</td>
<td>CoFe$_2$O$_4$</td>
<td>8</td>
<td>Photocatalytic activity; cytotoxic activity on MCF-7, CaCo$_2$, and NIH-3T3 cell lines</td>
<td>[58]</td>
</tr>
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<td>48</td>
<td>Aqueous solution of torajabin</td>
<td>Microwaves-assisted method</td>
<td>CoFe$_2$O$_4$</td>
<td>20–60</td>
<td>Photocatalytic activity; cytotoxic activity on MCF-7, CaCo$_2$, and NIH-3T3 cell lines</td>
<td>[59]</td>
</tr>
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<td>49</td>
<td>Caffeine</td>
<td>Coprecipitation</td>
<td>CoFe$_2$O$_4$</td>
<td>9</td>
<td>Drug release; cytotoxicity on U87 cell lines</td>
<td>[60]</td>
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<td>50</td>
<td>Glycyrrhiza glabra (licorice) roots</td>
<td>C. microphylla fruit extract</td>
<td>CoFe$_2$O$_4$ ferrofluid</td>
<td>13</td>
<td>Rheological behavior</td>
<td>[61]</td>
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<td>51</td>
<td>Caffeine</td>
<td>Coprecipitation</td>
<td>CoFe$_2$O$_4$</td>
<td>9</td>
<td>Drug release; cytotoxicity on U87 cell lines</td>
<td>[62]</td>
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<td>Tamarind extract</td>
<td>Coprecipitation</td>
<td>CoFe$_2$O$_4$</td>
<td>12</td>
<td>Photocatalytic activity; antibacterial activity against <em>E. coli</em>, <em>P. aeruginosa</em>, and <em>S. aureus</em> strains</td>
<td>[63]</td>
</tr>
<tr>
<td>53</td>
<td>Tamarind extract agar–agar from red seaweed (Rhodophyta)</td>
<td>Coprecipitation</td>
<td>CoFe$_2$O$_4$</td>
<td>13</td>
<td>AC conductivity</td>
<td>[64]</td>
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<td>54</td>
<td>Chenopodium album leaf extract</td>
<td>Coprecipitation</td>
<td>CoFe$_2$O$_4$</td>
<td>13</td>
<td>Photodegradation of organic pollutants</td>
<td>[65]</td>
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<td>55</td>
<td>Azadirachta indica leaves extract</td>
<td>Coprecipitation</td>
<td>CoFe$_2$O$_4$</td>
<td>13</td>
<td>Photodegradation of dyes</td>
<td>[66]</td>
</tr>
<tr>
<td>56</td>
<td>Coriandrum sativum extracts</td>
<td>Coprecipitation technique</td>
<td>Ni-doped cobalt ferrites</td>
<td>NA</td>
<td>Antioxidant activity; anticancer activity on MCF-7 cells</td>
<td>[67]</td>
</tr>
<tr>
<td>57</td>
<td>Verjuice extract</td>
<td>Sol–gel technique</td>
<td>CoFe$_2$O$_4$</td>
<td>NA</td>
<td>Anticancer drug (doxorubicin) delivery; anticancer activity on MCF-7 cells</td>
<td>[68]</td>
</tr>
</tbody>
</table>
Langmuir models. The adsorption process kinetics was established by the pseudo-second-order kinetic model. The composite was found to be an effective magnetic adsorbent for MG removal from water [38]. Leaf extract of medicinal plant Paederia foetida Linn. (Family: Rubiaceae) with rich phytochemicals like polysaccharides and phenolic compounds has been used as a stabilizing agent to prepare cobalt ferrite (CoFe₂O₄) using a hydrolyzing agent (urea) with 10–80 nm size. Furthermore, pronounced activity in oxidative degradation of MB and rhodamine B (Rhb) in the presence of H₂O₂ under solar irradiation was reported [39]. The catalytic potential of magnesium–cobalt ferrite (MgCoFe₂O₄) obtained using an aqueous extract of apple skins by green solubilization and the three-component condensation reaction of 1,3-dimethylbarbituric acid, aldehydes, and malononitrile to afford pyrano[2,3-d] pyrimidinedione and their bis-derivatives as a multicomponent reaction were demonstrated [40].

Many researchers reported the preparation of cobalt ferrite nanoparticles using phytochemicals derived from Mangifera indica leaf extract [41], methanol crude extract of rhizomes of Iraqi Rheum ribes [42], cashew gum (Anacardium occidentale) [43], sucrose, and olive leaf extract with the sol–gel autocondensation method [44] and apple cider vinegar (ACV) with the sol–gel autocondensation technique [45]. Further, rosemary extract/sucrose and its application on anticancer drug (doxorubicin (DOX)) delivery from CoFe₂O₄-tripolyphosphate-chitosan (CFO-TPP-CS) as well as effective against breast cancer cell line (MCF-7 cell) in an acidic medium was investigated [46]. The curd was used as "green" fuel for the preparation of nanostructured Zn-doped cobalt ferrites via combustion method with crystallite size in the range of 12–21 nm and identified its potential effect as photocatalyst for degradation of Congo red and Evans blue dyes under visible light. Antibacterial activity was inspected against both Gram-positive (S. aureus) and Gram-negative (Salmonella typhi) bacterial strains. S. typhi showed high antibacterial activity with the inhibition zone of Zn-doped CoFe₂O₄ (22 mm) compared to CoFe₂O₄ (16 mm) [47].

Two research groups independently implemented lemon juice as the green source; first, in accomplishing the synthesis of Samarium (Sm)-doped cobalt (CoFe₁₋ₓSmₓO₄) ferrite nanoparticles within the range of 10–22 nm by sol–gel autocondensation technique [48]. Second, a modified Pechini method using sucrose to exhibit excellent release of an anticancer drug (DOX) from CoFe₂O₄-polyethylene glycol (PEG)-DOX nanocomposite [49]. Besides these extensive investigations on synthesis and applications of green sources for the nanoparticles development, many inspired researchers used more numbers of diverse green sources for the nanoparticle synthesis such as the synthesis of nano-Co₈₀₋ₓNdₓFe₁₀₀₋₂₀xO₄ (CoNd) ferrites with various plant extracts (cardamom seeds, date fruits, flaxseed, tragacanth gum, lavender seeds, and moringa) using a sol–gel approach and these obtained nanoparticles were effective against S. aureus. The cervical cancer cells (HeLa) and human colorectal carcinoma cells (HCT-116) cell lines were used for anticancer activity by 4,6-diamidino-2-phenylindole (DAPI) and 3-[4,5-dimethylthiazol-2-yl]-2,5-diphenyltetrazolium bromide (MTT) assay. The result exhibited a significant decrease in cancer cell viability [50]. The fungi had the potential to yield an extensive array of treasures nanoscale materials. A simple method for the synthesis of cobalt ferrite nanoparticles using the fungus Monascus purpureus ATCC16436 cell-free culture filtrate was demonstrated. The obtained nanomaterial exhibited moderate antioxidant potential with IC₅₀ value of 100.25 μg mL⁻¹ against 25.31 μg mL⁻¹ of ascorbic acid by DPPH free radical scavenging activity in a dose-dependent manner. Antimicrobial assay was performed on bacterial strains (S. aureus ATCC6538, E. coli ATCC11229, Klebsiella pneumoniae ATCC13883, and P. aeruginosa ATCC15442) and fungal strains (Aspergillus niger, Alternaria solani, Fusarium oxysporum, and C. albicans ATCC10231) using agar well diffusion assay technique. MIC of the E. coli, S. aureus, P. aeruginosa, and K. pneumoniae was 250 and 500 μg mL⁻¹. MIC of the fungal species at 250 μg mL⁻¹ showed 14.53, 10.53, 11.76, and 9.53 mm inhibition zones of growth around the agar well for A. niger, A. solani, F. oxysporum, and C. albicans, respectively. It indicates that the synthesized nanoparticles exhibited a broad spectrum of antibacterial as well as antifungal activity by inhibiting the growth of all the tested species. Human breast carcinoma (MCF-7), hepatocellular carcinoma (HepG2), and normal human melanocytes (HFB-4) cell lines were selected for anticancer activity studies by MTT assay. The synthesized nanoparticles exhibited IC₅₀ values as 61.86, 45.21, and 200 μg mL⁻¹ against HepG2, MCF-7, and HFB-4, respectively. Results indicate concentration-dependent cell death with significant decrease in cell proliferation by increasing concentration [51]. Egg white, the natural polymer, is highly soluble in water, able to associate with metal ions in solution, and effective

<table>
<thead>
<tr>
<th>Sr. No.</th>
<th>Green reagent</th>
<th>Method used</th>
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<th>Size (nm)</th>
<th>Applications</th>
<th>References</th>
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<tr>
<td>62</td>
<td>Moringa oleifera leaf extract</td>
<td>NA</td>
<td>CoFe₂O₄/TiO₂ nanocomposite</td>
<td>7–11</td>
<td>Photocatalytic activity</td>
<td>[69]</td>
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<tr>
<td>63</td>
<td>Ginger root extract</td>
<td>Hydrothermal method</td>
<td>Cu-substituted cobalt ferrites</td>
<td>7–45</td>
<td>Photocatalytic activity</td>
<td>[70]</td>
</tr>
<tr>
<td>64</td>
<td>Elettaria cardamomum seed extract</td>
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<td></td>
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<td></td>
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</tr>
<tr>
<td>65</td>
<td>Baker’s yeast (Saccharomyces cerevisiae)</td>
<td></td>
<td>CoFe₂O₄</td>
<td>3–15</td>
<td>NA</td>
<td>[71]</td>
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</table>
binder cum gel to shape bulk and porous ceramics. Moreover, the egg white is also popular among researchers as a biotemplate for the green synthesis of cobalt ferrite [52–56]. Cobalt ferrite and nickel-substituted cobalt ferrites were afforded by herbal medicine, *Andrographis paniculata* (Acanthaceae) plant extract with 32 and 26 nm size, respectively. The clinical isolates of Gram-positive (*S. aureus* and *E. faecalis*) and Gram-negative (*P. aeruginosa* and *S. typhi*) bacterial strains were utilized for antibacterial studies. The tested nanoparticles exhibit a significant antibacterial effect against *S. aureus* (26 mm) at the concentration of 100 μg.mL⁻¹. Moreover, due to the narrow bandgap, prepared nanoparticles exhibited superior photodegradation of textile dyes (MB, RhB, Eriochrome black T, Rose Bengal, and Evans blue) under visible light to offer better choices for wastewater treatment application [57]. *Cydonia oblonga* extract was successfully utilized to get cobalt ferrite with a crystallite size of about 8 nm [58].

Aqueous solution of torajabin afforded 20–60 nm sized cobalt ferrite nanoparticles. Acid Orange 7 (AO7) dye was successfully degraded under sunlight exposure. The cytotoxic activity was investigated on breast cancer cell (MCF-7), colon cancer cell (CaCo₂), and mouse embryo fibroblast cell (NIH-3T3) cell lines using MTT assay. Pleasingly, tested nanoparticles were found to be nontoxic against cancer and normal cell lines [59]. Caffeine afforded an average particle size of 9 nm. MTT cytotoxicity assay was performed on the U87 cell lines (in a human primary glioblastoma cell line) [60]. Additionally, *Glycyrrhiza glabra* (licorice) roots [61], *C. microphylla* fruit extract [37], tamarind extract [62, 63], and ginger root extract [69], verjuice extract [68], *Moringa oleifera* leaf extract [69], *Coriandrum sativum* extracts [67], *Azadirachta indica* leaves extract [65], *Chenopodium album* leaf extract [66], *Elettaria cardamomum* seed extract [70], and baker’s yeast (*Saccharomyces cerevisiae*) [71] were successfully used for green synthesis of cobalt ferrite and related compositions.

### 3. Potential Applications of Cobalt Ferrite Nanoparticles

One can quickly agree with the significant importance of cobalt ferrite derived from green synthesis with numerous advantages in environmental and biomedical applications.

#### 3.1. Environmental Applications

**3.1.1. Metal Ions Detection/Removal for Environmental Remediation.** Traces of heavy metals and metalloids (enforce serious health hazards to humankind and aquatic life even at very low concentrations) are primarily responsible for water pollution, and have one of the global challenges. Conventional and nonconventional heavy metal removal, with multiple drawbacks, attracted attention to cobalt ferrite nanomaterials with adsorption properties. The cobalt ferrite exhibits high adsorption and sorption kinetics properties attributed to its unusual physicochemical behavior with the nanosize, shape, morphology, and a number of reactive sites on the surface through corners, edges, and defects [72]. Additionally, the formation of chemical bonding such as hydrogen bonding, the weak π–π or electrostatic interactions, ion-exchange phenomenon, and surface complexion is primarily responsible for the adsorption mechanism [73].

1. Using a similar mechanism of adsorption, manganese (II) ions from industrial wastewater were detected [41].
2. One environmental pollutant lead (Pb), being a highly toxic heavy metal, seriously affects human health with many diseases (alteration in physiological functions, neurological, respiratory, urinary, and cardiovascular disorders). The worldwide acceptable poisoning level for Pb in the blood is 10 μg/dl [74]. This dangerous environmental pollutant was successfully removed from polluted water via the adsorption mechanism of green cobalt ferrite nanomaterials [29].

**3.1.2. Photocatalytic Activity by Degradation of Dyes.** Among numerous synthetic dyes, many consist of toxic organic compounds and are majorly responsible for water pollution. Effluents from textile industries are significant contributors to dye pollution. Atmospheric and aquatic harmful organic components were effectively degraded using light sources like sunlight or UV light by semiconductor heterogeneous photocatalysts. Abundant reports in the literature proved the effectiveness of nanoferrite and their composites as photocatalyst through active free radical generation for the degradation of dyes [75]. Cobalt ferrites furnished from green synthesis efficiently degraded well-known dyes [64], specifically MB [56] RhB [39], Direct Red 81 [30], Congo red/Evans blue [47], anionic brilliant blue-R (BB-R) [55], and MG [38].

**3.2. Biomedical Applications**

**3.2.1. Antimicrobial Activity.** Human and animal health is always under threat from emerging, re-emerging, and persistence of microbial infectious diseases. Antimicrobial resistance (AMR) risk affects mankind’s health globally. Hence, many antibiotics and other antimicrobial medicines become ineffective and infections increase exponentially, leading to large numbers of death. Research on antimicrobial progressing swiftly with new strategies like nanomaterials. Nano-CoFe₂O₄ exhibited potent antimicrobial activity [61].

**3.2.2. Antibiofilm Activity.** Biofilm forming from a variety of microbial pathogens can pose a serious health hazard that is difficult to combat. Mostly, the existing antimicrobial agents failed to penetrate the biofilm; development of drug resistance and biofilm-mediated inactivation or modification of antimicrobial enzymes are the main drawbacks of conventional antibiotics [76]. Fortunately, nanocobalt ferrite exhibits antibiofilm-forming activity [36].

**3.2.3. Antioxidant.** Free radicals and reactive oxygen species (ROS) are detrimental to several tissues in the body, which invite many chronic health issues, including cardiovascular and inflammatory diseases, cataracts, and cancer. Nanomaterials can act as an antioxidant by preventing the formation or scavenging or
decomposition of radicals. Nanocobalt ferrites exhibit excellent antioxidant activity [51].

3.2.4. Magnetic Hyperthermal Therapy. Hyperthermia therapy, one of the treatment methods for cancer, generates higher-temperature tumors that can induce cancer cell death. Synthesis of multifunctional magnetic nanoparticles having the highest saturation magnetization with functionalized surfaces to attach to target tissues or cells selectively followed by applying heat with the help of an external alternating magnetic field has been an appealing area of research. The main concern lies with toxicity and duration to complete elimination of nanomaterial [77]. The quantity of energy dissipated by the nanomaterials per unit of the mass of the particles per unit of time is the specific absorption rate (SAR) or specific loss power. Hence, the estimation of temperature rise in response to the applied field indicates a particular loss of power (a very important magnetic property) which has a significant impact on the hyperthermic efficiency of magnetic nanomaterials. Nanocobalt ferrite was found to be an effective magnetic hyperthermia agent [21]. By far, nano-CoFe2O4 with high magnetic anisotropy is the most widely studied nanomaterials for hyperthermia therapy applications. Moreover, a tiny size of CoFe2O4, as compared with other ferrites, offers better heating efficiency [60].

3.2.5. Biocompatibility (Cytotoxicity, Cell Viability). Considering various biomedical applications, it is crucial to evaluate the biocompatibility of nanoferrite. Biocompatible material performs its desired action without adverse effects on the surrounding. The intensity of material that can cause damage to a cell is cytotoxicity, whereas cell viability is the number of healthy cells present. Effective biocompatibility of cobalt ferrite obtained by green synthesis is reported [54].

3.2.6. Anticancer Drug Delivery. Delivering anticancer drugs to a specific site for the result is a major challenge in present anticancer treatment. Nanomaterials have unique biological properties that allow them to bind, absorb, and carry anticancer drugs and imaging agents with high efficiency. Moreover, they can release the medicine in a controlled manner at a preselected biosite [78]. Cobalt ferrite was established as an effective drug delivery carrier; it was successfully demonstrated on anticancer drug (DOX) [46]. The applications of synthetic or green-mediated nanoparticles in biomedicine are immense [79, 80]. More investigations are warranted to understand their bioavailability, pharmacokinetics, and safety concerns.

3.2.7. Image Contrast Agents in MRI. The magnetic ferrite nanoparticles steered new advancements for specific imaging of cancer tissue and significantly contributed to the field of oncology [81]. The high distribution capacity and crystallinity offer to exhibit superior harmful contrast enhancements for target-specific tumor imaging that subsequently provide excellent imaging and targeting abilities for in vitro imaging applications [82]. In clinical use of MRI, cobalt ferrites induced high signal intensity of T2 contrast agents compared to iron oxide nanoparticles to diagnose many diseases in the liver and spleen for MR contrast agents [83]. Functionalized ferrite nanoparticles with suitable tumor-targeting ligands such as monoclonal antibodies, peptides, or small molecules help to precisely target and provide high contrast to tumor tissue. Appropriate manipulation to enhanced r2/r1 ratios, superior cytocompatibility, excellent hemocompatibility, and enhanced T1 and T2 relaxation time are ultimately responsible for in vitro MRI contrast enhancement [84]. Doping of metals such as manganese–zinc and gadolinium has shown high contrast in MRI [85, 86].

3.2.8. Biosensor. In high-performance clinical diagnosis, ferrite magnetic nanoparticles are popular biosensors. These biosensors require well-tuned physicochemical properties for probes detection to produce specific biological signals with minimal nonspecific binding. The factors primarily responsible for biosensing property are synthesis route, particle size, functionalization, sensitivity toward targeted intercellular biological molecules, and lower signal-to-noise ratio [87]. Cobalt ferrite biosensors with less magnetic susceptibility are capable of finding on-spot biomarkers in the biosamples. Excellent sensitivity, cheapness, high stability, great selectivity, and quick response at low temperature make cobalt ferrite sensors favorable for medical industries [88]. Moreover, it is expected to get enhanced biosensing properties of cobalt ferrite prepared using natural resources.

In one of the earliest clinical trials, polystyrene-coated iron oxide NPs were used to enhance MRI of the gastrointestinal tract (GIT). Since 1996, multiple nanoferrite compositions have been in clinical trials that have been approved by the Food and Drug Administration (FDA). Typical examples of coating agents include dextran/carboxyldextran in ferumoxtran, ferumoxide, and ferucarbotran; PEG in feruglose; and aminosilane in NanoTherm™. GastroMARK® utilizes siloxane-coated iron oxide NPs for MRI of the GIT. Ferumoxytol is a polyglucose-sorbitol-carboxymethyl-ether-coated γ-Fe2O3 that was developed and approved in the year 2000 as an MRI contrast agent for many cancers [89].

4. Challenges, Drawbacks, and Prospects

Although green synthesis of nanoscale cobalt ferrite has excellent potential, however, it possesses several challenges and drawbacks, such as availability/selection of specific material (complex extraction procedures, seasonal/regional availability of raw materials and their compositions), suitable synthesis conditions, quantity/quality control of the product (low purity and poor yield), and particular applications. These constraints pose difficulties in large-scale production adaptability/reproducibility (time and place of production) and industrial application of green-synthesized nanoscale cobalt ferrite. Therefore, selecting the best natural resource (cheap and commercially available raw material), applying large-scale feasible synthesis conditions, focusing yield improvement, achieving appropriate quality and size of nanoparticles, and employing simple energy-saving technology are a few of the research directions needed to be explored in the future. Therefore, it is anticipated that green synthesis of
nanoscale cobalt ferrite has a broad prospect and great potential for development.

5. Conclusion

Utilizing natural resources for green synthesis is a cutting-edge and flourishing area in exploring for enhanced environmentally favorable methods to afford nanoparticles. Using plant extracts or microorganisms for synthesizing nanoferrites is a more promising approach than conventional process. Considering broader applications of cobalt ferrite in biomedical and environmental remediations, we compiled recent developments on green synthesis of simple and mixed nanocobalt ferrite with distinct applicational advantages.

Data Availability

The data used to support the findings of this study are available from the corresponding author upon request.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

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