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Review Article

The Role of Phytochemicals in the Management of Periodontal Diseases

Areej Hasan S. Al dhaher [1] **and Nawal Al Hakawati** [2]
[1]Department of Anatomy, College of Medicine, University of Basrah, Basrah, Iraq.
[2] Biological Sciences Department, Faculty of Science, Beirut Arab University.

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Abstract

According to the World Health Organization (WHO), about 10%-15% of the population is affected by periodontitis. This complex infectious condition arises from the aggressive growth of bacteria on the teeth. Both surgical and nonsurgical treatment options are available to manage MB formation. Consistent daily care and regular professional intervention can prevent the condition from worsening and lead to significant improvements in oral health. However, these conventional treatments often face restrictions due to adverse effects and antibiotic resistance, prompting the exploration of alternative therapies. This review evaluated the therapeutic effect of phytochemicals in managing periodontal disease and highlighted the mechanisms by which compounds exhibit anti-inflammatory, antimicrobial, and antioxidant effects. Some promising herbal agents, such as Baccharis Dracunculifolia, Piper nigrum, Punica grtiatum, and Scrophularia Striata, have been reported to be effective in reducing plaque accumulation and other periodontitis indications, sometimes comparable to standard treatments. In addition, natural products can modulate the oral microbiome and enhance tissue enhancement. In addition, the review explained the crucial role of PROs, satisfaction, and QoL in contemporary health care. Although the patient's perceptions of its benefits are often favorable, clinical evidence by the absence of large-scale trials. The significant challenges of using natural NPation include a lack of product standardization and inconsistent study designs with short follow-up periods. Future research will require standardized, long-term randomized test guidelines to establish sthe success and safety ofherbal interventions in the management of periodontitis.

Corresponding Author: Areej Hasan S. Al dhaher, Branche of Anatomy, College of Medicine, University of Basrah, Basrah, Iraq
Email: areej.saleem@uobasrah.edu.iq

1. INTRODUCTION

Periodontal disease is a chronic inflammatory disease affecting the skeleton of the teeth; as a consequence, the alveolar bone and gums [1]. periodontal diseases include dental plaque–induced gingivitis, chronic periodontitis, aggressive periodontitis, necrotizing periodontal diseases, and periodontitis as a manifestation of systemic conditions [2], [3]. These conditions vary in severity but share common features of an aggregate of bacterial biofilm is the leading cause of gingivitis, which causes periodontitis if left unrefined[4]. Long gingivitis progression promotes chronic periodontitis, which can lead to loss of the bone and ligament [5]. Loss of load-bearing periodontal structures and eventual tooth loss are characteristic features of advanced periodontitis. Furthermore, necrotizing periodontal diseases represent a more severe, acute form of infection typically associated with compromised host immune systems [6]. Globally, severe periodontitis affects approximately 10–15% of the adult population, with prevalence increasing markedly with age [7]. The rising rate of periodontal diseases correlated with modifiable and non-modifiable factors. Smoking, Poor oral hygiene, and diabetes mellitus are modifiable risk factors, while age and heredity are non-modifiable risk factors. In addition, many factors affect periodontal diseases, such as low educational level and low income below the federal poverty line [3]. Periodontitis is also associated with whole-body disorders such as diabetes, vascular disease, respiratory disease, rheumatoid arthritis, and Alzheimer's disease. Similarly, pregnancy and depression [4],[8]- [9]. Other systemic diseases may be related to periodontal inflammation, such as a correlation between oral anaerobic bacteria and colon cancer. Malignant inflammatory infections in the human intestinal tract may be caused by migration and colonization of *Fusobacterium nucleatum*, which is associated with periodontal disease [10].

1.1 CONVENTIONAL TREATMENTS FOR PERIODONTAL DISEASES

Periodontal therapy is structured in three sequential phases: nonsurgical treatment, corrective surgical therapy, and supportive maintenance care [11]. Each phase addresses distinct clinical objectives while integrating mechanical and pharmacologic interventions to achieve optimal outcomes [15]. Scaling and root planning (SRP)

are nonsurgical interventions that are central to nonsurgical periodontal therapy, considered the most important methods for managing chronic periodontitis.

Scaling removes supragingival and subgingival deposits, while root planning eliminates contaminated cementum and dentin surfaces, thereby reducing microbial load and preventing recolonization [16]. The adverse effects of scaling and root planning include pain, root sensitivity, bleeding, gingival contour changes, and rare treatment failure [17]. Antibiotic therapy is administered either systemically or through localized delivery systems. Systemic antibiotics offer broad-spectrum coverage but have limitations due to low site-specific concentrations, patient compliance requirements, and risk of resistance and side effects, such as vomiting, allergic reactions, and nausea [18]. Local antimicrobial agents—such as minocycline gel, chlorhexidine chips, and doxycycline—demonstrate superior site-specific efficacy with reduced systemic exposure; however, local antibiotics come at the cost of temporary improvement and potential pathogen recolonization [19].

Corrective Therapy (Surgical Phase) The surgical phase aims to optimize access for debridement, correct anatomically undefined deficiencies, and reconstruct lost periodontal tissues. These interventions improve gingival morphology, promote patient-driven oral hygiene, and restore function and esthetics [20]. Supportive Therapy and Maintenance Supportive Periodontal Therapy (SPT) is vital for preventing disease recurrence and ensuring compliance with oral hygiene for long-term disease control. Successful SPT depends on regular clinical reassessment [21].

2. RATIONALE OF USING NATURAL PRODUCTS

Conventional treatments typically include mechanical debridement, antibiotics, and surgical interventions; however, these methods may have limitations, such as antibiotic resistance and patient discomfort [6]. Compounds derived from plants, fungi, and other undefined biologic undefined sources have been commonly used in phytotherapy for their antimicrobial, anti-inflammatory, and healing properties [22]. In modern dentistry, natural compounds such as curcumin, green tea polyphenols, and propolis have shown promising effects in inhibiting periodontal pathogens, reducing oxidative stress-induced tissue damage, promoting healing and regeneration of periodontal structures, and reducing plaque formation [23], [24]. Their biocompatibility and potential synergistic effects with conventional therapies make them attractive alternatives or adjuncts in periodontal treatment [25]. Crocin, isolated from the flowers of Crocus, showed intense activity in managing periodontitis [26]. Its pharmacologic activity is primarily related to its propensity to diminish oxidative stress and attenuate inflammation. In addition, it plays a role in modulating bone metabolism by balancing osteoclast and osteoblast activity and enhancing type I collagen production in dental and osseous tissues [26]. Recent research has shown that an ecofriendly natural hydrogel of 30% licorice extract with anti-inflammatory and antibacterial properties can help cure oral ulcers in rats. The formulation demonstrated significant therapeutic effects by tissue regeneration, collagen anabolism, enhanced growth factor, and substantial reduction in inflammatory markers (88%) [27]. An in vivo study assessed a 2.5% garlic mouthwash and found that it sustained reduced levels of total oral bacteria. However, participants reported adverse effects—namely, an unpleasant taste and halitosis [28]. In a clinical trial, participants using neem *Azadirachta indica* mouthrinse experienced significant reductions in gingival index scores and probing depths compared with those using a placebo [29]. FLJ has garnered interest as a potential treatment for dry mouth because of its ability to raise salivary pH and stimulate saliva flow with potent anti-inflammatory and antioxidant activities. High-dose and topical formulations of curcumin improve oral lichen planus because of their potent antioxidant, anti-inflammatory**,** and antimicrobial activities [31].

In addition to their antimicrobial and anti-inflammatory properties, natural products may have a positive impact on patient reported outcomes (PROs), satisfaction, and overall quality of life (QoL) [32]. Compared with conventional treatments, such as chlorhexidine or systemic antibiotics, which are frequently linked to tooth staining, altered taste, mucosal irritation, or gastrointestinal discomfort, herbal agents typically cause fewer side effects [32], [33]. This decrease in adverse effects can improve patient comfort and therapy adherence [32]. Phytochemicals may enhance everyday functioning and perceived oral health by lowering inflammation, bleeding, halitosis, and oral discomfort—symptoms closely associated with functional and psychosocial QoL domains [33], [34]. Furthermore, patients frequently believe that herbal therapies are safer, more natural, and culturally acceptable, which increases their level of satisfaction and willingness to stick with their treatment [32], [35], [36].

Therefore, this review aims to examine the role of natural products in managing periodontal disease, focusing on their antibacterial, anti-inflammatory, and regenerative properties, evaluating current evidence from preclinical and clinical studies supporting their efficacy, and discussing challenges and future directions in integrating natural therapies into periodontal care.

3. MECHANISM OF ACTION OF NATURAL PRODUCTS IN MANAGING PERIODONTITIS

To understand the mechanisms by which phytochemicals contribute to the management of periodontitis, it is essential to examine their chemical structures. Identifying structure–activity relationships help explain their antimicrobial, anti-inflammatory, and antioxidant properties, which are responsible for their therapeutic effects in periodontal treatment.

3.1Flavonoids : Flavonoids are a diverse group of naturally occurring polyphenolic compounds that are abundant in fruits, vegetables, and medicinal herbs. They are characterized by a common 15-carbon skeleton (C6–C3–C6) structure [37]. Based on variations in the oxidation state and substitution patterns of the C-ring, such as saturation and the presence of carbonyl groups, flavonoids are classified into several major subclasses, including flavanones, flavanols, isoflavones, flavones, flavanols, flavanonols, anthocyanidins, and chalcones/dihydrochalcones [38].

Previous studies have demonstrated the beneficial effects of flavonoids on gingival fibroblasts, periodontal ligament fibroblasts, and osteoblasts [39].

These compounds exert anti-inflammatory activities by modulating pathogen-associated molecular pattern (PAMP)-induced signaling pathways, particularly through interference with Toll-like receptor (TLR) signaling [39]. For example, epigallocatechin gallate (EGCG) inhibits TLR4-mediated MyD88- and TRIF-dependent signaling cascades and suppresses IκB kinase activity [40], [41]. Similarly, quercetin interferes with MyD88-dependent pathways [42], while isoliquiritigenin attenuates interferon regulatory factor (IRF) phosphorylation in RAW 264.7 murine macrophages stimulated with TLR3 and TLR4 agonists [42]. Moreover, myricetin suppresses ERK1/2, p38 MAPK, and AKT signaling pathways, reduces IL-1β production, and inhibits lipoteichoic acid-induced COX-2 expression and NF-κB activation [43], [44]. Naringenin, a flavanone, has also been shown to inhibit TLR2 signaling by preventing IκB degradation and reducing JNK phosphorylation [45].

3.2 Essential Oils: Essential oils (EOs) are volatile, hydrophobic, and aromatic compounds derived from plants [46], [47]. Their constituents originate primarily from terpenoid and phenylpropanoid biosynthetic pathways and encompass a wide range of chemical classes, including aldehydes, ketones, phenols, and nitrogen-containing compounds. Essential oils capture the characteristic aroma and flavor of plants and exhibit diverse biological activities, including antimicrobial, anti-inflammatory, and antioxidant effects [46], [47]. Bouhdid et al. (2009) [48] demonstrated that the essential oil of *Origanum compactum* disrupts bacterial membrane integrity by dissipating potassium-ion gradients, resulting in the loss of membrane potential in *Pseudomonas aeruginosa*. Additional studies revealed that this oil causes cell wall disruption in both *Escherichia coli* and *Bacillus subtilis* [49]. These structural alterations are associated with reduced ATP synthesis at the bacterial membrane [49]. Likewise, the essential oil of *Melaleuca alternifolia* induces potassium leakage and suppresses respiratory activity in *E. coli* [50]. Allaker and Douglas (2009) reported that essential oil-based mouthwashes eliminate microorganisms through multiple mechanisms, including disruption of the early plaque biofilm matrix, inhibition of essential bacterial enzymes, damage to the bacterial cell wall, suppression of bacterial replication, and induction of endotoxin leakage [51]. Furthermore, Batista et al. (2014) [52] demonstrated that α-bisabolol, azulene, matricine, and chamazulene—major terpenoid constituents of *Matricaria recutita* volatile oil—exhibit significant antibacterial, anti-inflammatory, and antispasmodic activities.

3.3 Alkaloids: Alkaloids are naturally occurring nitrogen-containing compounds that typically possess heterocyclic ring structures composed primarily of carbon, hydrogen, and nitrogen, with occasional incorporation of sulfur or oxygen atoms [53]. Both in vitro and in vivo studies have demonstrated that alkaloids possess a broad spectrum of biological activities, including antiviral, anticancer, and anti-metastatic effects against various oral diseases and malignancies [54]. Berberine, an alkaloid isolated from *Coptidis rhizoma*, has exhibited potent antibacterial activity against *Actinobacillus actinomycetemcomitans* and *Porphyromonas gingivalis*, while also reducing their collagenase activity [55]. In addition, berberine inhibits oral pathogenic microorganisms and exerts anti-inflammatory effects through modulation of cytokine production [56]. Lu et al. (2012) [57] demonstrated that berberine suppresses inflammation by targeting the NF-κB signaling pathway. Specifically, it binds to IκB kinase (IKK), inhibiting its activity and preventing the phosphorylation and degradation of IκBα, the endogenous inhibitor of NF-κB. As a result, NF-κB remains sequestered in the cytoplasm and is unable to translocate into the nucleus, thereby reducing the transcription of pro-inflammatory cytokines such as TNF-α, IL-1β, and IL-6. Moreover, Palchykovska et al. (2013) [58] suggested that epiberberine may contribute to periodontal disease management through its antiviral properties. Its proposed mechanisms include inhibition of viral adsorption and entry into host cells, as well as suppression of viral genome expression.

3.4 Tannins: Tannins are polyphenolic compounds widely distributed in the bark, wood, leaves, fruits, roots, and seeds of many plant species. They possess a strong ability to bind proteins and various mineral ions [59]. Tannins exhibit a broad range of biological activities, particularly antibacterial and anti-inflammatory effects. Gallotannins have been reported to help prevent dental caries through inhibition of human salivary amylase activity. Irfan et al. (2017) [60] suggested that the condensed tannins and epigallocatechin gallate (EGCG) present in Triphala formulations may contribute to enhanced gingival healing. EGCG binds to bacterial cell walls and inhibits their biosynthesis, thereby suppressing bacterial proliferation. In addition, EGCG inhibits proteases and collagenases, protecting collagen fibers from enzymatic degradation while promoting collagen synthesis [61], [62]. Punicalagins, a group of ellagitannins isolated from *Punica granatum*, have been identified as potent inhibitors of matrix metalloproteinases (MMPs), thereby preserving collagen and other extracellular matrix components. Furthermore, they reduce the production of pro-inflammatory cytokines such as IL-1β and TNF-α, helping to limit tissue destruction and inflammatory responses [25]. A mouthwash containing *Terminalia chebula* fruit extract, which is rich in tannins and possesses antibacterial properties, demonstrated effectiveness comparable to chlorhexidine in controlling plaque accumulation and improving gingival health after four weeks of use, although tooth staining and altered taste perception were reported as side effects [63], [64].Farha (2020) [65] described three principal antibacterial mechanisms of tannins: disruption and inhibition of bacterial cell wall synthesis, iron chelation, and interference with fatty acid biosynthesis pathways. Additionally, tannins can modulate the expression of bacterial virulence factors, including adhesins, biofilm formation, motility, and extracellular enzymes.

4. PROVE FROM AN INVESTIGATIVE STUDY SUPPORTING THE USE OF HERBAL PRODUCTS

Numerous clinical trials have demonstrated the therapeutic potential of natural products, including herbal extracts, polyphenols, and probiotics, in the management of various conditions ranging from oral and inflammatory diseases to cancer and metabolic disorders. Table 1 summarizes selected clinical studies that have investigated the efficacy of herbal remedies in the treatment and management of periodontitis.

Table 1: Summarized of some clinical studies evaluating herbal extracts for the treatment of periodontitis recorded by the author from references [66–81].

plant name	Form of use	indication	Method of application	effectiveness	Ref.
Nigella stavia oil	Mouthwash (in vivo)	Chronic periodontitis	Underwent scaling and root planning	PL index, CAL, BOP Improved	[66]
Punica grtiatum And *Piper nigrum*	Irrigation solution (in vivo)	Chronic periodontitis	Irrigation by using pulsated irrigation device, Waterpik	PL; significant reduction BoP; irrigation with CHX shows better result and pocket depth reduced	[67]
Sassurea lappa	Irrigation solution (in vivo)	Chronic periodontitis	Subgingival irrigation, an adjunct agent	Show better result than CHX, dramatic decrease in pocket , and pus discharge was seen	[68]
Neem gel	Gel	PL, GI and detection of oral bacterial count	1 gm of gel and put in by finger, twice daily	Improvement of PL, GI, reduced of oral bacterial count with no side effect	[69]
Scrophularia Striata	Mouthwash (in vitro)	Chronic periodontitis	Mouthwash, followed up after two week and four weeks	Better result than standard compared to Iranian mouthwash, and effective in treating	[70]
Baccharis dracunculifolia	Mouthwash (in vivo)	Plaque and dental caries	As a mouth rinse	Comparable to standard mouthwash, there is an improvement in caries and PI	[71]
Ficus religiosa, Glycyrrhiza glabra, and *Plantago* major	Ethanol extracts (*in vitro*)	Plaque and periodontal pathogens	Antimicrobial efficacy test	Antibacterial activity	[72]
Morinda Citrifolia (noni fruit)	Mouthwash (in vivo)	Periodontal diseases	Used as mouth rinse	Treat bacterial infections	[73]
Zataria multiflora	Mouthwash (in vitro)	Plaque	used as a mouthwash against isolated bacteria	Showed antibacterai activity	[74]
Salvadora persica	Mouthwash (in vivo)	Plaque	Tooth cleaning and use the mouthwash three time daily	Inhibit plaque formation	[75]
Aloe vera	Gel	Pocket depths depending on stage II to IV and grade A or B.	Applied after 1 week of supportive therapy	PPD reduction CAL gain and other indexes	[76]
Olive oil	Solution	Pocket depths depending on stage II to IV and grade A or B.	Unique application in hygiene phase	PPD reduction CAL gain and other indexes	[77]
Triphala: Emblicaofficinalis Terminalia belerica Termina liachebula	mouthwash .	Chronic periodontitis: The GI and PI at baseline, 7, 30	Mouthwash, for 45 day two times a day	GI and PI improvment.	[60]
Arrabidaea chica Verlot	Gel	Oral Mucositis	Use the gel 3times a day, under the tongue palate and cheek.	The safety of the herbal gel and improvement of clinical study (phase 2)	[78]
Camellia sinensis	As a beverage	Chronic periodontitis: PPD, BOP, PL	Daily drinking	Reduce PPD, BOP	[79]
Septilin (a herbal immunomodulatory agent) A combination of different extract	dietary supplementation	Chronic periodontitis	Dietary supplementation for 3 weeks	Improved GI, BOP and PPD	[80]
powders of *Azadirachta indica, Vaikranta bhasma and Ajamoda satva,* and *extracts of Punica granatum ,Zanthoxylum alatum, Vitex negundo, Acacia arabica, Triphala and Embelia ribes*	Dental cream with herbal ingredients	PL, GI oral hygiene status, bleeding index,	Use dental cream for six weeks	reduction in PL, GI, oral hygiene index, and microbial. With safty to use	[81]

PL: Plaque Index) / CAL: Clinical Attachment Level/ BOP: Bleeding on Probing

Gingival Index (GI) , CHX: Chlorhexidine, PPD: Probing Pocket Depth

5. IMPACT OF NATURAL PRODUCTS ON PATIENT OUTCOMES, SATISFACTION AND QUALITY OF LIFE

Recent shifts in healthcare have emphasized not only clinical outcomes but also patient-reported outcomes (PROs), which are defined by the U.S. Food and Drug Administration (FDA) as direct reports from patients regarding their health status without interpretation by clinicians. In addition, oral health–related quality of life (OHRQoL) has become an important measure, reflecting the physical, emotional, and social impacts of oral conditions on daily functioning and overall well-being. This patient-centered approach highlights the importance of incorporating patients' experiences, expectations, and preferences into treatment planning, particularly in dentistry [82]. Patients' perceptions of natural and conventional dental therapies vary depending on their personal experiences and the specific oral condition being treated. The perceived safety, accessibility, and convenience of herbal remedies have contributed to growing interest in their use [83]. A survey involving 500 participants reported that approximately 70% used phytotherapeutic products, such as herbal mouthwashes and toothpastes, while 65% rated their experience as satisfactory or highly satisfactory [84]. Despite the increasing popularity of phytotherapy in oral healthcare, studies evaluating consumer acceptance, satisfaction, and long-term adherence remain limited [83].

In both intervention and observational clinical trials, quality QoL has been was assessed objectively. The effects of phytotherapy on QoL compared with control treatments or placebo showed varied outcomes. Despite this variability, within each study's parameters, patients, clinicians, and community members generally expressed favorable views of phytotherapy's clinical benefits, its impact on QoL, its accessibility, and its cost-effectiveness according to Shinkai et al. (2024) study [32]. These perceptions reinforce the relevance of phytotherapy in patient-centered care.satisfaction, and better adherence[32]**.** Most participants considered phytotherapy remedies as their desired—or only—option for oral care. A separate clinical trial found the herbal formulation less practical than a low-cost control that required no expert training [85]. Although laboratory and preclinical research highlight the potential of herbal extracts against periodontal infections, well-designed clinical trials remain rare [32]. Strengthening this evidence base is essential to fully understand the impact of phytotherapy on PROs, patient satisfaction, and QoL.

6. CHALLENGES, LIMITATION AND FUTURE DIRECTION

Potential Challenges in using natural products in periodontal therapy are a lack of standardization, as many herbal formulations suffer from inconsistencies in concentration, purity, Study Design, and bioavailability. This variability makes it challenging to ensure that patients receive a uniform therapeutic dose or formulation, which is crucial for predictable clinical outcomes. Also, it is important to prevent the contamination and authentication of herbal ingredients [86]**.** Additionally, a few clinical studies reported the activity of herbal remedies and randomized controlled trials (RCTs) for long duration that can improve the effectiveness of using these treatments [87]. Also, it is important to find a standard protocol to ensure bioavailability. Several factors limit the use of herbal products in periodontal care. Treatment approaches remain narrow, with most studies targeting initial non-surgical therapy and only a few examining supportive periodontal therapy or herbal monotherapy. Follow-up periods are generally brief—up to six weeks—resulting in limited long-term data and highlighting the need for standardized, extended observations. Inconsistent reporting of key clinical parameters such as plaque levels, gingival bleeding or inflammation, and overall periodontal status is essential for future comparative studies [88]. Finally, Future research should aim to compare the outcomes of different adjunctive herbal products across various stages of periodontitis [89].

7. CONCLUSION

Periodontal disease, a multifaceted condition driven by microbial imbalance and chronic inflammation, presents significant challenges in management due to limitations of conventional therapies. Natural products play a crucial role in periodontitis management through their antimicrobial, anti-inflammatory, and antioxidant effects. They suppress pathogenic bacteria, inhibit inflammatory cytokines, and promote tissue healing, making them valuable alternatives to conventional treatments like chlorhexidine and corticosteroids. Despite these advantages, challenges persist, including variability in bioactive compound concentrations, non-standard procedures, and short-term follow-up data. Additionally, bioavailability and optimal delivery systems require refinement to maximize therapeutic impact. Nevertheless, natural products offer safer, cost-effective, and culturally acceptable adjuncts or alternatives to conventional therapies, aligning with the growing demand for holistic and preventive dental care [90]. To translate this potential into clinical practice, future research must prioritize rigorous, large-scale trials, standardized extraction methods, and innovative formulations. Integrating these evidence-backed natural therapies into mainstream periodontal management could revolutionize oral healthcare, bridging traditional wisdom with contemporary scientific validation for sustainable patient outcomes.

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CONFLICTS OF INTEREST

No conflicts of interest relevant to this article.

ETHICS

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BIOGRAPHIES OF AUTHORS

Dr. Areej Hasan S. Aldhaheris is an Associate Professor at the College of Medicine, University of Basrah. She built her academic foundation in Biology at the University of Basrah, earning both her Bachelor's and Master's degrees. She then pursued and obtained her PhD in Biology with a specialization in the Phytochemistry of natural products from the University of Surrey in the United Kingdom. Her primary research expertise lies in the field of natural products, focusing on the purification and identification of pure compounds from natural sources and evaluating their biological activity through various bioassays. Dr. Aldhaher has actively contributed to her field, authoring several scientific papers that have been presented at national and international conferences and published in reputable journals. Her email address is areej.saleem@uobasrah.edu.iq.

Dr. Nawal Al Hakawati is an Associate Professor of Physical Biochemistry in the Biological Sciences Department. She received her PhD from the University of Surrey in United Kingdom in 2017 where she worked on Synthesis and Physicochemical Characterizations of Calix-macrocycles with their Analytical and Biological applications. She currently serves as a Visiting Research Fellow at the same institution within the School of Chemistry and Chemical Engineering, and is a Board Member of the Women and Inclusion in Supramolecular Chemistry International network. Dr. Al Hakawati has lectured at several universities in Lebanon. Her interdisciplinary research focuses on Supramolecular Chemistry and Environmental Technology, with an emphasis on advancing innovative and sustainable solutions. Her email address is n.elhakawati@bau.edu.lb