# The Benefits of *Murraya koenigii* in Dentistry – A Scoping Review

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Oral diseases are among the most common long-term conditions affecting the population. Medicinal plants are being used as a natural remedy for oral health issues due to their medicinal properties and lower side effects and cost compared to conventional antibacterial and anti-inflammatory agents. This study aims to review and summarize the potential uses of Murraya koenigii (L.) Spreng. (syn. of Bergera koenigii L.) in dentistry and update clinicians about its implications in dental management for maintaining oral health. The data was collected by five reviewers from multiple articles, case reports, review papers, and original studies that were published in PubMed, Web of Science, and Scopus. The extracts of Murraya koenigii is a promising alternative to synthetic therapeutic agents in dentistry. Further research is required to explore its potential use in oral health.

Keywords: Antimicrobial; Bergera koenigii L; herbal extract; Murraya koenigii; Oral health.

Oral health is integrally linked to general well-being. It has a significant impact on individual lives with regards to quality of life. Oral disorders are among the most prevalent chronic diseases affecting people due to their incidence, impact on people and society, and cost of treatment. Consequently, they are regarded to be an important public health concern.<sup>1</sup>

To prevent oral diseases, good oral hygiene is important. The most effective oral hygiene practices suggest employing both chemical and mechanical methods to control plaque. However, the growth of resistant microbes rendering them ineffective because of their prolonged use.<sup>2</sup> The most used antiplaque agent is chlorhexidine gluconate. The use of chlorhexidine has some potential drawbacks like altered taste sensation, staining of teeth, and development of resistant bacteria that incapacitate its application on long term basis.<sup>3</sup> There exists a need to develop some innovative strategies that act against oral diseases. One such technique is to investigate the abundant therapeutic plants found in nature. Plant remedies provide naturally available active substances that act against dental diseases including dental caries, gingivitis, and periodontal diseases and restore the general health with minimal harmful effects and maximum efficiency.<sup>4</sup> Natural herbs, whether used alone or in combination, be both safe and beneficial in the treatment of a variety of oral health conditions.<sup>2</sup> As the plant extracts have their therapeutic qualities such as antibacterial,

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analgesic, antioxidant, and anti-inflammatory they may be a good alternative to conventional drugs for the treatment of gingival and periodontal disorders when used as an adjuvant.<sup>5</sup>

According to the World Health Organisation, over 80% of the global population currently seeks primary health care and wellness from traditional healing practices and herbal remedies. A significant portion of the general population in many developed nations maintains traditional medical practices, using medicinal plants.<sup>6</sup>

Ayurveda, or traditional Indian medicine, and traditional Chinese medicine are two of the most prominent living traditions that persist to this day. These two medical systems have been combined to produce a wide range of knowledge about medicinal plants. Both may have aided in the regulation of herbal medications in the pharmacy sector.<sup>7</sup> Among them, Murraya koenigii, a synonym of Bergera koenigii L and known as a curry leaf, is one of the traditional herbal plants that belongs to the Rutaceae family (Figure 1).8 It is a tiny, scented, semi-deciduous shrub or tree is extensively grown in South-East Asia, certain regions of the United States, and Australia, but it is native to the east and south of India, Pakistan, Sri Lanka, and China.9 The name of the species honors Johann König, a botanist. The genus Murray honors Johann Andreas Murray, a Swedish physician and botanist. As a result, the curry leave's botanical name is Murraya koenigii.10 The usage of curry leaves is employed in Indian Ayurvedic and Unani treatments. They are a natural flavouring ingredient with several health advantages. The leaves of Murraya koenigii's are used in small amounts for their unique fragrance and potential to ease digestion owing to the presence of volatile oil. They are commonly used to flavour meals in Asian cuisines. The leaves have a bitter, little pungent, and mildly acidic flavour, and even after drying, the leaves retain their flavour and other features.<sup>11</sup>

The presence of phytochemical constituents gives it medicinal properties as antiinflammatory, antibacterial, anti-fungal, antiulcer activity, antiemetic, antioxidant, anti-carcinogenic, anti-diabetic, and hepato-protective characteristics. It also has other pharmacological activities such as cholesterol-lowering properties, heart activity, phagocytic activity, and cytotoxic action.<sup>12</sup> Some of the important bioactive components of the plant are summarised in Table 1.<sup>13</sup> Because of its pharmacology and phytochemistry, it is not only utilised as a nutritional supplement but also as an ayurvedic medication with therapeutic potential for treating a variety of illnesses both individually and in combination with other herbs in formulations.<sup>14</sup>

A comprehensive review documented the advantages of this traditional medicine in dentistry. In treating postoperative complications following dentoalveolar surgeries, it highlighted the benefits of several herbal extracts, such as Arnica Montana, Binahong Bromelain, Aloe-vera, Curcumin, Pisidium guajava, Calendula, Pomegranate, Chamomile flower, green tea, Passiflora incarnata, Propolis, and Hypericum perforatum.<sup>15</sup> However, another review focused on the pathophysiology, triggering events, antecedents, and mediators of periodontitis, a chronic inflammatory disease of the periodontal tissues. It also explored novel strategies for preventing and treating periodontitis using propolis, probiotics, and various herbal extracts.16

Reviews of the available literature are very helpful in clinical decision-making. Previous literature studies describe the *Murraya koenigii* and explain its effectiveness with various medicinal properties. The present review aims to evaluate the the potential uses of *Murraya koenigii*. Considering the paucity of research in this area, the present scoping review is mainly based on articles taken from published literature research and review articles, based on a specific set of key words which emphasized on the published information about *Murraya koenigii*, its potential uses along with its limitations in the field of dentistry.

#### **Research Question**

To review and summarize the current research on the potential uses of *Murraya koenigii* in Dentistry.

#### MATERIALS AND METHODS

The database was thoroughly searched for the duration between January 2013 to December 2023. The data was compiled from original *in vitro* and clinical studies, case reports and review papers published in Web of Science, PubMed, and Scopus, as well as other general publications which are related to the subject matter. The relevant

articles were extracted by using different keywords such as 'herbal plant,' 'dentistry,' 'murraya,' and 'curry leaf.' The full text articles published only in English language and the articles discussing the use of *Murraya koenigii* leaves in dental treatment were included in the study (Figure 2). Whereas the articles written other than English language, unpublished data, and unrelated studies were excluded. The data obtained from various articles on *Murraya koenigii* plant were thoroughly reviewed and an attempt was made to reach insightful conclusions. Key points mentioned in the articles about the curry leaf plant are summarized in Table 2.<sup>17-77</sup>

#### **RESULTS AND DISCUSSION**

The phytochemical analysis of various plant parts such as leaves, stem barks, flowers, fruits, roots and aerial part have been studied and proved to have several compounds. Various extraction methods have been tried using ethanolic, methanolic, aqueous, chloroform, benzene, hexane etc. The compounds found in the stem bark were meranzin hydrate, epoxyosthol, isomeranzin, and murracarpin<sup>17</sup>, sugar and starch<sup>38</sup> cyclic monoterpenoid pyranocarbazole alkaloids such as murrayazolinol, murrayakoeninol and bicyclomahanimbine.<sup>45</sup>

Compounds found in leaves were phenols, murrayatanineonyl compounds,<sup>18</sup> carbohydrates, proteins, steroids, saponins, quinones, alkaloids, flavonoids, tannins, and volatile oils<sup>22,26</sup> arborinine, ferulic acid, umbelliferone, mahanimbine, koenimbine, koenidine and O-demethyl murrayanine<sup>24</sup>, lipid and protein in leaf,<sup>38</sup> mahanimbine, girinimbine, murrayacine, murrayanine, murrayafoline A, 3-methylcarbazole pinene, caryophyllene, sabinene, phellandrene, terpinene and myrcene<sup>52</sup>, murrayatanine-A, bismahanimboline <sup>62</sup>, high content of moisture, proteins, fats and oils, more levels of vitamin B1, B2, B3, and C with lower levels of vitamins A and E. The mineral elements of Fe, Na, Fe, Mn, K, Cu, Ni 68 and including the existence of specific chemicals such as fatty acids, á-terpineol, eucalyptol, stigmasterol, ethyl cinnamate, and epiyangambin.69 Compounds detected from leaf oil were Linalool, Elemol, Geranyl acetate, Myrcene, Allo-Ocimene, á-Terpinene, and (E)-â-Ocimene and Neryl acetate<sup>42</sup> sabinene, caryophyllene, á-pinene, terpinen-4-ol, â-pinene, ã-terpinene, á-terpinene, (E)-nerolidol, á-humulene, limonene, myrcene, â-elemene, â-selinene, and á-thujene.<sup>70</sup> **Antiplaque properties** 

Many medicinal plants such as *P. guajava*, *Eucalyptus, A. nilotica, M. koenigii L.S* and *H. sabdariffa L* have been studied against different organisms such as *Streptococcus salivarius*, *Streptococcus mutans* and *Streptococcus sanguis*. Primary plaque colonizers can potentially be inhibited by all these herbal extracts including *M. koenigii L.S.*<sup>27</sup>Whereas, another study demonstrated the effectiveness of polyherbal mouthwash containing *Murraya koenigii, Acacia nilotica, Psidium guajava*, and *Eucalyptus hybrid* was beneficial in preventing dental caries and plaqueinduced dental disorders.<sup>33</sup> However, in treating plaque-induced gingivitis *M. koenigii* mouthwash had the same effectiveness as chlorhexidine.<sup>75</sup>

A study in which *Murraya*, chlorhexidine, and placebo groups were compared and results showed statistically significant difference in gingival scores as compared to baseline, whereas *Murraya* and chlorhexidine were statistically significant in plaque scores.<sup>77</sup> Another research found that extracts from common plants like *Cassia alata*, *Terminalia chebula*, *Acalypha indica*, and *Cadaba fruticosa*, as well as medicinal plants like *Mentha longifolia*, *Cuminum cyminum*, and *Murraya koenigii*, significantly inhibited the formation of biofilms by isolated strains from natural environments.<sup>39</sup>

#### Analgesic properties

At present, there have been no published human trials to prove the analgesic qualities of the plant. However, some studies have been documented on animal models. Among them, one of the studies experimented on rats and mice, in which the results revealed a considerable decrease in the number of writhing when Murraya koenigii leaves were hydroalcoholically extracted as compared to Coriandrum sativum leaves. They also proved that an increased dosage of the leaf extract from M. koenigii was equivalent to a conventional dose of tramadol.47 In vivo models were utilised in another study, in which, a rat forced swim test and a barbiturate-induced sleeping duration model were used to assess the central nervous system stimulating activity, while the analgesic effect was evaluated using tail-flick and hot-plate test techniques. The study results demonstrated that the *M. koenigii* leaves have analgesic and central nervous system stimulating effects.<sup>48</sup>

#### Antimicrobial properties

Murraya Koenigii Leaves was screened against various microorganisms by using several extraction methods. The antimicrobial action against Candida albicans, Escherichia coli, Pseudomonas aeruginosa, and staphylococcus aureus was assessed by using methanolic Extract 59,60,65,74 of Murrava Koenigii leaves and it also markedly suppressed the main virulence key factors of Candida albicans, including filamentation, cell surface hydrophobicity, yeast-to-hyphal transition, formation of biofilm, and hemolysin synthesis.60 The extract of M. koenigii with methanol showed better inhibitory effects against Staphylococcus aureus. It claims to be due to significantly high total phenol, flavonoid content in the plant.<sup>71</sup> When compared to the conventional drug Kanamycin, the methanolic extract of pyranocarbazoles found in the plant, such as koenine, koenigine, and mahanine, showed strong antibacterial action against the bacterial strains Streptococcus aureus and Klebsiella pneumonia. Only koenigine was discovered to be effective against a range of Candida species.72

Whereas, both methanol and ethanol extracts of the plant produced antimicrobial effects

Table 1. Bioactive components of Murraya koenigii.

S.	Bioactive Components	Formula
No.	-	
1.	Murrayazolinol	C <sub>23</sub> H <sub>25</sub> NO <sub>2</sub>
2.	Bicyclomahanimbicine	C <sub>22</sub> H <sub>25</sub> NO
3.	Umbelliferone	Č H <sub>6</sub> O,
4.	Mahanimbine	C <sub>22</sub> H <sub>25</sub> NO <sub>2</sub>
5.	Koenimbine	$C_{10}^{23}H_{10}^{23}NO_{2}^{2}$
6.	Girinimbine	C <sub>18</sub> H <sub>17</sub> NO
7.	Murrayacine	$C_{18}H_{15}NO_{2}$
8.	Murrayanol	$C_{24}^{10}H_{29}^{10}NO_{2}^{2}$
9.	Murrayanine	$C_{14}H_{11}NO_{2}$
10.	Isolongifolene	C <sub>15</sub> H <sub>24</sub>
11.	Murrayafoline A	$C_{14}H_{13}NO$
12.	3-methylcarbazole	$\dot{C}_{12}\dot{H}_{11}N$
13.	Koenigine	$C_{10}H_{10}NO_{2}$
14.	Sabinene	C <sub>10</sub> H <sub>16</sub>
15.	á-pinene	$C_{10}^{10}H_{16}^{10}$

towards strains of *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Candida tropicalis*, and *Candida parapsilosis*.<sup>74</sup> Another research formulated and tested the topical cream comprising *M. koenigii* extract. The antibacterial properties of the ethanol extract of *M. koenegii* leaves were assessed against *S. aureus*,<sup>28,29,74</sup> *S. epidermidis*, and methicillin-resistant *S. aureus* and *S. epidermidis*. A concentration-dependent analysis of the extract showed strong antibacterial property towards the examined species.<sup>28</sup> The optimal concentration for reducing *Candida albicans* growth was found to be the ethanol extract from *Murraya koenigii* leaves, which was incorporated into an ointment with 12.5% and 25% concentrations.<sup>23</sup>

The beneficial health effects of ethanolic extract of M. koenigii has been proved after assessing its antimicrobial and antioxidant properties against Escherichia coli, Klebsiella pneumoniae, Staphylococcus aureus, Salmonella paratyphi and Pseudomonas aeruginosa.<sup>29</sup> The methanolic extracts of curry leaves from Balai ringai, Bau, and Kuching have antibacterial properties towards S. aureus, while those from Balai ringai are also effective against E. coli.41 When ethanolic extract of curry leaf was tested for antibacterial activity against Porphyromonas gingivalis, it showed a substantial bactericidal activity in comparison to clove and cinnamon.44 Another study results showed that the ethyl acetate leaf extract demonstrated superior antibacterial efficacy against Vibrio alginolyticus, Vibrio parahaemolyticus, Staphylococcus aureus, Escherichia coli, Listeria monocytogenes, Yersinia enterocolitica, Salmonella typhi, and Salmonella paratyphi.<sup>54</sup> Murraya koenigii leaves' hydro-distilled essential oil was tested for its antimicrobial and antioxidant properties. Regarding Corynebacterium TB, Klebsiella pneumonia, Pseudomonas aeruginosa, Enterobacter aerogenes, and Streptococcus pyogenes, the oil exhibits a maximal zone of inhibitory ability.42 Plant roots were screened phytochemically using ethanol, petroleum ether, chloroform, and ethyl acetate extracts to identify flavonoids, alkaloids, steroids, and carbohydrates existence in it. All these extracts from the M. koenigii root were found to have antimicrobial action towards Pseudomonas aeruginosa, Bacillus subtilis, S. aureus, Micrococcus luteus, Aspergillus niger, and Escherichia coli.67 The compounds

S. No.	Article details	Type of study	Findings
1.	Hossain et al. <sup>17</sup> (2016)	Phytochemical analysis	The study found four distinct compounds: murracarpin, epoxyosthol, isomeranzin, and meranzin hydrate
2.	S Sharmila et al. <sup>18</sup> (2013)	Phytochemical analysis	Phenol, cardiac glycoside carbonyl compounds and terpenoids were detected in <i>M.koenigii</i> .
3.	Wadanambi et al. <sup>19</sup> (2022)	Computational study	By inhibiting the Main protease catalytic activity, koenine, o-methylmurrayamine A, mukonicine, and girinimbine may be able to limit SARS-CoV-2 replication.
4.	Sampath et al. <sup>20</sup> (2022)	Phytochemical analysis	<i>Murraya koenigii</i> leaves contained a novel dimeric carbazole alkaloid that showed considerable inhibitory activity against both á-amylase and á-glucosidase, suggesting potential uses as an antidiabetic drug.
5.	Sinha N <sup>21</sup> (2019)	In vitro study	Curry leaf extract with water:70% ethanol demonstrated the strongest ability to scavenge free radicals.
6.	Shalini R <sup>22</sup> (2013)	Phytochemical analysis	The plant may be considered for the therapy of cardiovascular disorders due to its thrombolytic, cytotoxic, and antioxidant gualities.
7.	Lubis M. F et al. <sup>23</sup> (2014)	Animal study with in vitro experimental	The ethanol extract of <i>Murraya koenigii</i> leaves can be an be safely used in ointments and the most effective doses to prevent the growth of <i>Candida albicans</i> were found to be 12.5% and 25%.
8.	Tahia F et al. <sup>24</sup> (2015)	Phytochemical analysis	The compounds as ferulic acid, umbelliferone, arborinine, koenimbine, mahanimbine, <i>O</i> -demethyl murrayanine, and koenidine were isolated from the plant.
9.	Qin-Ge Ma et al. <sup>25</sup> (2015)	Phytochemical analysis	By using the 2,2-diphenyl-1- picrylhydrazyl (DPPH) assay, chemical components present in the leaves demonstrated considerable antioxidative properties.
10.	Gupta et al. <sup>26</sup> (2018)	<i>In vitro</i> study and Phytochemical analysis	The study found that the extract of <i>M. koenigii</i> was high in carbohydrates, alkaloids, flavonoids, steroids, proteins, glycosides, and tannins.
11.	Chandrashekar B R et al. <sup>27</sup> $(2014)$	In vitro study	Primary plaque colonization can be prevented by <i>M</i> koenigii
12.	Dash G K et al. <sup>28</sup> (2017)	In vitro study	The plant extract exhibited good antibacterial activity against the investigated microbes in a concentration -dependent manner.
13.	Kavitha M. <sup>29</sup> (2017)	In vitro study	The variety of <i>M. koenigii</i> plant grown locally have antibacterial and antioxidant properties that benefit human health.

# Table 2. The data obtained on Murraya koenigii

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14.	Iman V. <sup>30</sup> (2016)	<i>In vitro</i> experimental and in vivo animal study	By triggering apoptosis and reducing inflammation, the compound gerinimbine present in the plant may have chemopreventive or chemotherapeutic effects
15.	J. Patterson <sup>31</sup> (2015)	<i>In vitro</i> study	Curry leaf has less harmful effects on liver cells and may be useful in preventing colon cancer
16.	Sriram et al. <sup>32</sup> (2019)	In vitro study	The study demonstrated the anti-inflammatory activities of <i>M. koenigii</i> ethanol extracts. The extract fractions prevented the denaturation of albumin due to heat and served as inhibitors of free radicals.
17.	Shekar et al. <sup>33</sup> (2018)	In vitro study	The growth of <i>F. nucleatum</i> and <i>P. gingivalis</i> was inhibited by the plant extract
18.	Saleem A. et al. <sup>34</sup> (2022)	Animal study	The molecular docking study results demonstrated that the main sources of cytotoxic and antioxidant chemicals are n-hexane and ethyl acetate fractions. Additionally, there are molecular interactions between MCL-1, Bclxl, and Bcl-2 anti-apoptotic proteins and newly found phenolics from plant shoot fractions.
19.	Zahin M. <sup>35</sup> (2013)	In vitro study	The phenol-rich benzene fraction exhibits potential antioxidant and antimutagenic properties.
20.	Parithy et al. <sup>36</sup> (2021)	In vitro study	The antioxidant effects were higher with the ultrasonic assisted extraction (UAE) of <i>M. koenigii</i> leaves compared to solvent and microwave assisted extractions.
21.	B.R Chandrashekar et al. <sup>37</sup> (2019)	In vivo clinical study	Both chlorhexidine polyherbal groups showed no statistically significant difference in <i>S. mutans</i> and total viable counts, post intervention plague build-up.
22.	Vijayvargia P. <sup>38</sup> (2016)	Phytochemical analysis	The highest levels of lipid and protein were found in the leaf, while the levels of starch and sugar were found be more in the stem. It had been demonstrated the greatest DPPH radical scavenging capacity of the leaves.
23.	Madathil D. <sup>39</sup> (2015)	Phytochemical analysis with <i>in vitro</i> study	The formation of biofilm was significantly inhibited by the plant's extracts.
24.	Tomar R.S. et al. <sup>40</sup> (2017)	Phytochemical analysis	Both young and old leaves showed the presence of phenols and scavenging activity.
25.	Yee Khin Than et al. <sup>41</sup> (2023)	Phytochemical analysis	The existence of tannin, terpenoids, flavonoids, alkaloids, and saponin were demonstrated by the phytochemical screening of the extracts. The antimicrobial effects were shown

26.	Priya et al. <sup>42</sup> (2014)	Phytochemical analysis with <i>in vitro</i> study	by the curry leaves methanolic extract from Balai ringai, and Bau towards <i>S. aureus</i> and the extract of leaves from Balai ringai was effective against <i>E. coli</i> . The significant chemical substances found in the essential oil of <i>M. koenigii</i> leaves were Linalool, Allo-Ocimene, Geranyl acetate, Elemol, Myrcene, Neryl acetate, (E)-â-Ocimene and á-Terpinene. The oil exhibits a high zone of inhibition towards <i>Pseudomonas</i> <i>aeruginosa, Klebsiella pneumonia,</i> <i>Enterobacten earogene Commebacterium</i>
27.	Kumari et al. <sup>43</sup> (2019)	In vitro study	<i>Enteroducter derogenes</i> , <i>Coryneodctertum tuberculosis</i> , and <i>Streptococcus pyogenes</i> . Following the encapsulation process, in an aqueous medium, petroleum ether extract of curry leaves and its carbazole compounds demonstrated
28.	Nakao et al.44 (2021)	In vitro study	higher antioxidant activity. Curry leaves extract showed better bactericidal activity against <i>Porphyomonas gingivalis</i> by causing
29.	Ahmad K. et al.45 (2015)	Phytochemical analysis	bacterial membrane depolarization. The study identified three cyclic monoterpenoid pyranocarbazole alkaloids such as murrayazolinol.
30.	Salvi and Choudhary <sup>46</sup> (2020)	In vivo animal study	murrayakoeninol and bicyclomahanimbine from n-hexane extract of <i>M. koenigii</i> bark. The <i>in-vivo</i> tissue distribution in albino rats revealed that formulations accumulated in distinct organs. Prolonged release of the natural medicing from the carrier system
31.	Salwe et al. <sup>47</sup> (2018)	In vivo animal study	reduces the size of the doses and the frequency. There was a noticeable decrease in the amount of writhing when <i>Murraya</i> <i>koenigii</i> leaves extract was used. An increased dosage of leaf extract was equivalent to a conventional dose
32.	Brind L. et al. <sup>48</sup> (2014)	In vivo animal study	of tramadol. In <i>in vivo</i> models, it has been shown that an ethanol extract of <i>M. koenigii</i> leaves stimulates the central nervous
33.	Nalli Y. et al. <sup>49</sup> (2016)	<i>In vitro</i> and <i>in vivo</i> study	system and analgesic activities. Murrayakonine A, O-methylmurrayamine A, and murrayanine were found to be the most effective in reducing IL-6 and TNF-á release, as well as decreasing the production of LPS-induced TNF-á and IL-6 in human peripheral blood mononuclear cells. The chemicals girinimbine and 1-hydroxy-7-methoxy -8-(3-methylbut-2-en-1-yl)-9H-carbazole

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34.	Rahayu <sup>50</sup> (2019)	<i>In vitro</i> study	-3-carbaldehyde were highly effective against <i>Bacillus cereus</i> . Additionally, koenimbine and murrayamine J were effective against <i>Staphylococcus aureus</i> . The secondary metabolites present in the methanolic extract of curry leaves such as terpenoids, saponins, alkaloids, tannins. and flavonoids were responsible for the significant DPPH scavenging
35.	Aslam I. <sup>51</sup> (2017)	Phytochemical analysis and <i>in vitro</i> study	activity. The volatile compounds isolated from identified from <i>M. koenigii</i> plant were caryophyllene, pinene, myrcene, sabinene, terpinene, and phellandrene. They demonstrated better antibacterial activity against strains of <i>Escherichia coli</i> , <i>Micrococcus luteus</i> , <i>Pasteurella multocida</i> , and <i>Bacillus subtilis</i>
36.	Pujan N. et al. <sup>52</sup> (2020)	Computational study	The evaluation of cytotoxicity on a breast cancer cell line revealed that the phytochemical's presence in leaf, stem, and root components emphasizes its function as a COX 2 inhibitor.
37.	Engwa et al. <sup>53</sup> (2016)	<i>In vitro</i> and <i>in vivo</i> study	An aqueous and ethanol extracts of <i>Murraya koenigii</i> showed good antioxidant activity due to the presence of flavonoid and flavanol. This could be attributed to the medicinal properties of the plant
38.	Abuga I. et al. <sup>54</sup> (2020)	<i>In vitro</i> study	Following treatment with plant extract, the bacteria's cellular morphology altered including changes in their organisation, stiffness, and membrane disintegration. Ethyl acetate leaf extract showed higher antibacterial effects towards <i>Staphylococcus aureus, Listeria</i> <i>monocytogenes, Vibrio parahaemolyticus,</i> <i>Vibrio alginolyticus, Yersinia enterocolitica,</i> <i>Escherichia coli, Salmonella typhi</i> and <i>Salmonella paratyphi</i>
39.	Jayaraman et al. <sup>55</sup> (2021)	Phytochemical analysis and <i>in vitro</i> study	<i>Murraya koenigii</i> revealed a high amount of phenol concentration. <i>Murraya koenigii</i> demonstrated the highest level of radical scavenging activity.
40.	Sharma A. et al. <sup>56</sup> (2023)	In vitro study	Zinc oxide nano particles synthesised from the aqueous extract of <i>Murraya</i> <i>koeingii</i> showed significant cytotoxic and antidiabetic activity, as well as antimicrobial and antioxidant activity.
41.	A. Patil R.et al. <sup>57</sup> (2021)	<i>In vitro</i> study	The alkaloids derived from the pet ether extract of <i>Murraya koenigii</i> have demonstrated high antioxidant properties. The dopaminergic activity was significantly reduced in validated animal models such as haloperidol- induced catalepsy in mice, apomorphine

			-induced stereotypic behaviour, foot shock-induced aggression, and phenobarbitone-induced sleeping behaviour. This may be due to the carbazole alkaloids with antioxidant
42.	K Rangasamy and E. Namasivayam <sup>58</sup> (2014)	In vitro study	properties. As lsolongifolene compound exhibited its strong scavenging properties, it can be considered an effective antioxidant for patients suffering from numerous oxidative degenerative disorders such
43.	Tirumalasetti J.et al. <sup>59</sup> (2014)	In vitro study	as cancer. The methanolic extract of <i>Murraya</i> <i>koenigii</i> showed its antibacterial effects against <i>Pseudomonas aeruginosa</i> , <i>Escherichia Coli</i> , <i>Klebsiella</i> , <i>staphylococcus aureus</i> and
44.	Muthamil S, and Karutha Pandian S. <sup>60</sup> (2016)	In vitro study	Canaida albicans. The important virulence characteristic features of <i>Candida</i> <i>albicans</i> including filamentation, cell surface hydrophobicity, yeast-to- hyphal transition, and biofilm were significantly reduced by the methanolic leaf extract of <i>M. koenieii</i>
45.	Rohan S. et al. <sup>61</sup> (2018)	<i>In vitro</i> study	Both aqueous and methanolic extracts of <i>Murraya koenigii</i> have demonstrated the strongest antidiabetic effect in the yeast glucose uptake method as well as DPPH free radical scavenging activity. Curry leaves have been shown to be a good natural source of chemicals that are both antidiabetic and antioxidative, helping to lower blood sugar levels and prevent oxidative damage.
46.	SP. Tan et al. <sup>62</sup> (2017)	Phytochemical analysis and animal study	The MTT assay demonstrated the cytotoxic effect of murrastinine-C and murrayatanine-A compounds against HL-60 and HeLa
47.	Rou Chian Ng et al. <sup>63</sup> (2018)	In vitro study	In cupric reducing antioxidant capacity (CUPRAC), it was discovered that chloroform extract of M <i>urraya koenigii</i> stem bark had the highest antioxidant activity. The most potent antioxidant agent was discovered to be mahanimbine, a bioactive molecule from <i>Murraya</i> <i>koenigii</i> 's stem bark extract.
48.	Abeysinghe D. T. et al. <sup>64</sup> (2021)	Review	<i>M. koenigii</i> is an abundant source of bioactive metabolites. Natural origin, low cost, and few side effects have drawn scientist's attention to produce nutraceuticals and plant-based medications
49.	Uma Maheswari N and Cholarani N. <sup>65</sup> (2013)	Phytochemical analysis and <i>in vitro</i> study	The methanolic extract of <i>M. koenigii</i> has shown superior antibacterial effects against <i>Staphylococcus aureus</i> , and

662	SHIVAKUMAR et al.	, Biomed. & Pharmacol. J,	Vol. 17(2), 653-670 (2024)
			<i>Pseudomonas aeruginosa</i> followed by <i>E. coli, Proteus vulgaris</i> , and <i>Bacillus subtilis</i> . A qualitative screening revealed the presence of amino acids. In <i>Proteus vulgaris</i> , strong antioxidant capacity has
50.	Heeralal et al. <sup>66</sup> (2022)	Phytochemical and <i>in vivo</i> animal study	been observed. Curry leaves are highly helpful to rats in decreasing and preventing the damage caused by exposure to chlorpyrifos. They are a rich source of phenolic, alkaloids, and flavonoids and also show antioxidant and antimutagenic action
51.	Vats, M. et al. <sup>67</sup> (2011)	Phytochemical analysis and <i>in vitro</i> study	Phytochemical testing of the root extracts of the plant showed the existence of steroids, alkaloids, flavonoids, and carbohydrates. According to the study, chloroform, ethyl acetate, petroleum ether, and ethanol extracts have remarkably strong antibacterial properties. Extracts of petroleum ether and chloroform also exhibited antifungal
52.	Uraku and Nwankwo <sup>68</sup> (2015)	Phytochemical analysis	<i>Murraya koenigii</i> leaves were low in saponins and carotenoids and rich in flavonoids, alkaloids, and tannins. Proximate analysis results indicated a low level of crude fibre and carbohydrates, but a comparatively high level of moisture, lipids and oils, proteins, and ash. The vitamin composition results showed low amounts of vitamins A and E and high levels of vitamins B1, B2, B3, and C. The components of the mineral elements revealed the existence of Fe, Na, Fe, Mn, K, Cu, and Ni. All mineral values, except for zinc, which is 40 mg/day, are below accentable ranges
53.	Moni S S et al. <sup>69</sup> (2021)	Phytochemical and spectral analysis	The study revealed the presence of tannins, fatty acids, steroids, and alkaloids. The extract contained special compounds like stigmasterol, epiyangambin, eucalyptol, ethyl cinnamate, á-terpineol, steroids, and fatty acids.
54.	Verma, R S et al. <sup>70</sup> (2013)	Phytochemical analysis	Some of the main constituents of the essential oils included á-humulene, á-thujene, (E)-nerolidol, â-selinene, â-elemene, caryophyllene, terpinen-4-ol, ã-terpinene, â-pinene, á-terpinene, and limonene. Different chemotypes of <i>M. koenigii</i> were discovered in populations from the Western Himalayas when the current data were compared to those from previous investigations.

55.	D.T. Abeysinghe et al. <sup>71</sup> (2021)	Phytochemical analysis	For the first time, the study reported elevated sabinene levels in <i>M. koenigii</i> . <i>M. koenigii</i> demonstrated the best
		and <i>in vitro</i> study	inhibitory effect against Staphylococcus aureus. The study found that <i>M.</i> <i>koenigii</i> had a significantly large overall phenol and flavonoid content, as well as increased antioxidant and antibacterial activities.
56.	Joshi T. et al. <sup>72</sup> (2017)	Phytochemical isolation and <i>in vitro</i> study	Koenine, Koenigine, and Mahanine compounds from the plant showed higher antibacterial activities as compared to the standard drug Kanamycin against <i>Klebsiella pneumonia and</i> <i>Streptococcus aureus.</i> The compound that proved effective against a range of <i>Candida species</i> was only koenigine.
57.	N. Anjaneyulu et al. <sup>73</sup> (2017)	Phytochemical analysis	Key phytochemicals found in <i>Murraya</i> <i>Koenigii</i> may have the desired medicinal implications, such as anti-microbial, anti-inflammatory, anti-diabetic, anti-ulcer, anti-fungal, and cosmetic applications.
58.	Katoch A et al. <sup>74</sup> (2013)	Phytochemical analysis and <i>in vitro</i> study	The methanol and ethanol extracts of the plant produced considerable zones of inhibition towards <i>Staphylococcus aureus</i> , <i>Pseudomonas aeruginosa</i> , and <i>Candida tropicalis</i> , and <i>Candida parapsilosis</i> . The aqueous extract of <i>Murraya koenigii</i> leaves contained tannins and both the alcoholic extracts showed the presence of quinones, coumarin, and sugar.
59.	Varghese, et al. <sup>75</sup> (2018)	A randomized controlled clinical trial	<i>M. koenigii</i> mouthwash had the similar effects in treating plaque-induced gingivitis as chlorhexidine.
60.	Gupta A and Purohit A <sup>76</sup> (2018)	A randomized controlled clinical trial	For both the curry leaf and the chlorhexidine mouthwash groups, there was a statistically significant difference in the mean salivary pH, whereas the mean tongue pH was only significant in the curry leaf mouthwash group.
61.	Verma, et al. <sup>77</sup> (2022)	A randomized double blinded controlled trial	<i>M. koenigii</i> , 0.2% chlorhexidine, and placebo mouthwash showed a statistically significant difference in gingival scores when compared with baseline. There was statistically significant difference in plaque scores for <i>M. koenigii</i> and chlorhexidine groups of $0.878 \pm 0.433$ and $1.090 \pm 0.613$ , respectively. However, between <i>M. koenigii</i> , chlorhexidine, and placebo groups, the mean change was not statistically significant.in gingival and plaque index scores.



Fig. 1. Murraya koenigii plant

obtained from the hydro-distillation method of *M. koenigii* leaves such as caryophyllene, pipene, phellandrene, sabinene, myrcene, and terpinene have significant antibacterial activities when tested against *Bacillus subtilis*, *Pasteurella multocida Micrococcus luteus*, and *Escherichia coli*.<sup>51</sup> Furthermore, another study assessed the individual and synergistic effects of ethanolic extracts of, *Murraya konigii*, *Eucalyptus hybrid*, *Psidium guajava* and *Acacia nilotica* extracts, as well as their combinations, on *P. gingivalis* and *F. nucleatum*. The combined forms of all the plant extracts were effective in preventing the growth of these bacteria.<sup>33</sup>

# **Antiviral properties**

As the carbazole alkaloids such as o-methylmurrayamine A, mukonicine, girinimbine and koenine, are rich in *Murraya koenigii*, one of the computational studies investigated its



Fig. 2. PRISMA Diagram (flowchart)

potentiality in restricting SARS-CoV-2 replication by inactivating the main protease catalytic activity.<sup>19</sup>

# Anti-inflammatory properties

One study isolated the carbazole alkaloids O-methylmurrayamine A, murrayanine, and murrayakonine A from equal ratio of chloroform and methyl alcohol extracts of leaves and stems of Murraya koenigii (Linn.) Spreng and assessed their anti-inflammatory properties. Results have shown that all the compound effectively inhibiting Interleukin-6 and Tumour Necrosis Factor- á and showed their declined production induced by Lipopolysaccharide in human peripheral blood mononuclear cells.<sup>50</sup> Another animal study evaluated the anti-inflammatory effects of the chloroform, petroleum ether, and ethanol extracts of Murraya koenigii on the male Wistar rats by conducting acute carrageen induced paw oedema and yeast induces hyperpyrexia methods. Among them, the anti-inflammatory properties were seen better with the ethanol extract of M. koenigii. 32

## Antioxidant properties

Curry leaves have high levels of flavonoids, alkaloids, and phenolic compounds, and they also have antioxidant properties.<sup>66</sup> M. koenigii has an isolongifolene molecule, which is a strong antioxidant that can be recommended to patients with oxidative degenerative disorders such as cancer.58 It was discovered that Murraya koenigii has a high total phenol concentration. Murraya koenigii demonstrated the greatest capacity for radical scavenging.55 The highest levels of sugar and starch were found in the stem, whereas the highest levels of protein and lipids were found in the leaf, according to primary metabolites. It was discovered that DPPH radical scavenging ability was greater in leaves.<sup>38</sup> In a study, phytochemical testing revealed the existence of many phytoconstituents with in the aqueous and ethanolic extracts of Murraya koenigii, including proteins, carbohydrates, steroids, phenols, quinones, alkaloids, volatile oils, flavonoids, saponins, and tannins. This adds to Murraya koenigii's thrombolytic, cytotoxic, and antioxidant potential characteristics.<sup>22</sup> Strong DPPH scavenging activity was demonstrated by the methanolic extract of curry leaf <sup>50, 61</sup> including the aqueous extract.<sup>61</sup> This could be due to the presence of saponins, terpenoids, tannins, alkaloids and flavonoids.50

Another study determined the greatest free radical scavenging action of curry leaves water:70% ethanol extraction compared to absolute ethanol, hexane, and water.<sup>21</sup> Whereas, in an aqueous solution, petroleum ether extract and its carbazole components demonstrated superior antioxidant activity.<sup>43</sup>

The chloroform extract of stem bark of the plant was found to possess the highest antioxidant activity in cupric reducing antioxidant capacity. This could be mainly because of presence of most active antioxidant compound mahanimbine that has been separated from the Murraya koenigii's stem bark.63 By using ultrasonic assisted extraction method, leaves of the plant demonstrated higher antioxidant activities as compared to microwave assisted and solvent assisted extraction methods.36 The study that used Murraya koenigii pet ether extract and alkaloids isolated from it in an animal model also showed strong antioxidant activity.57 Furthermore, in both in vitro and in vivo assessment on albino Wistar rats, it has been demonstrated that, the ethanol and water extracts of Murraya koenigii exhibited antioxidant activity due to more flavanol and flavonoid contents.53

#### **Anticancer properties**

A carbazole alkaloid called Girinimbine extracted from M. koenigii, was shown in a study to reduce the cellular viability of human colon cancer cells without having any harmful effects on normal cells and reduction of inflammation. Additionally, it also reduced inflammation in zebrafish embryos, with a considerable distribution of apoptotic cells observed following a 24-hour treatment period.30 The leaf has been also proved to be very effective in the prevention of human colon cancer while causing minimal toxic effects to liver cells.<sup>31</sup> The phytochemical, girinimbine present in leaf, stem and root parts of the plant has been proved to have anti-inflammatory properties by employing random forest models and molecular docking to interact with the COX-1 and COX-2 enzymes, free energy calculations and dynamics simulation. Cytotoxicity testing on a breast cancer cell line revealed that the presence of girinimbine compound supports its action as a COX-2 inhibitor.52 Curry leaf oil contains high levels of vitamin A and calcium, making it beneficial for bone health, osteoporosis, calcium shortage, and cancer therapies such as radiation and chemotherapy.78

#### Others

A novel dimeric carbazole alkaloid derived from Murraya koenigii leaves has shown remarkable inhibitory effects on á-amylase and á-glucosidase in vitro, suggesting potential therapeutic use as an antidiabetic drug.<sup>20</sup> An in vitro investigation using zinc nanoparticles (ZnO NPs) from Murraya koenigii's aqueous leaf extract showed moderate antibacterial and freeradical scavenging activity in addition to strong antidiabetic and cytotoxic effects.56 Furthermore, a study that used Murraya koenigii's methanolic and aqueous extracts revealed that both had the strongest antidiabetic effect when tested using the yeast glucose uptake method. Curry leaves therefore demonstrated an excellent natural supply of antidiabetic and antioxidant chemicals to lower blood sugar and prevent oxidative damage.62 In addition to this, another animal study on albino rats found that murrayanol, an active ingredient present in the plant can quickly achieve and maintain high drug concentrations in the bloodstream, making them beneficial for treating diabetes mellitus. In albino rats, it showed that the formulations accumulated in various organs, and the natural drug was released from the carrier system over an extended period, resulting in a reduction in both quantity and frequency of doses.<sup>46</sup> In a study where Murray koenigii leaves were fractionated in phenolic-rich benzene, it showed excellent wide-ranging antioxidant properties including antimutagenic effects against Salmonella typhimurium.35

# **Future recommendations**

Despite the numerous challenges addressed in the medicinal plant-based drug discovery process, the natural compounds from *Murraya koenigii* will continue to be a crucial part of the research for novel medications. Although the plant has been extensively studied in medicinal field, it remained to be fully explored in in dentistry. Additionally, the literature contains very little information about human trials using various extraction techniques. It is recommended to ascertain the effective dose of each plant portion with its corresponding chemicals for upcoming clinical trials. Studies involving synergistic effects between *Murraya konegii* and other herbal plants should be conducted.

#### CONCLUSION

Based on the literature search and their results, it can be concluded that nature is the greatest creative pharmacist and might have the key to healing every illness. The plant's natural components have produced several therapeutically beneficial remedies. They have been proven to have the medicinal properties with all types of their extracts. From this review, we discovered that Murraya possesses many characteristic features that are beneficial in the field of dentistry. This is mainly due the presence of phytochemicals or secondary metabolites in this herbal plant that are effective against various microbes and oral diseases. Hence, it could be a promising safer alternative to synthetic antimicrobial agents for further use.

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# **Conflict of Interest**

There are no conflicts of interest.

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#### **Author Contributions**

VHS, AV: concept, designed the protocol; VHS, AV, EH: collected the data, analysed, and interpreted; VHS, AST, AV: manuscript preparation and editing; EH, AV, NMZ: editing and reviewthe final manuscript. Finally, all authors had given approval for manuscript publication.

# Data availability statement

Data will be available on request.

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