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Melatonin: A Naturally Derived Molecule as a Protector of Oral Health

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Abstract
Melatonin is an indole amine that is an evolutionarily conserved molecule and is ubiquitously present in all living beings on this earth. In plants, melatonin is a protector of oxidative stress and improves photosynthesis while in animals and humans, it is a regulator of the biologic clock , anti-inflammatory, antioxidant and cytoprotective molecule. Melatonin is found in saliva, oral tissues and has a significant impact on preventing the progression of oral diseases such as dental caries, periodontal disease and oral premalignant lesions. Melatonin has been tried in topical and systemic formulation for management of oral diseases. This chapter recommends the consumption of melatonin rich fruits, vegetables and herbs as a source of melatonin for the prevention of oral disease. The chapter highlights the usefulness and benefits of melatonin and details the plant and herbal sources of melatonin and sheds evidence on how the use of these botanical products could improve oral health status of patients.

***Keywords*:** Antioxidant, anti-inflammatory, cytoprotective, dental caries, melatonin, oral cancer, periodontitis, saliva

24.1 Introduction

Oral diseases denote a broad term to include numerous conditions that affect the oral cavity also known as the stomatodeum. The oral cavity encompasses a number of anatomical

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structures such as the upper and lower jaw bones, teeth and their supporting apparatus, the tongue, hard and soft palate, buccal mucosa, lips and the associated salivary glands. It is understood that the principal functions of the oral cavity include aiding in mastication, phonation, swallowing and respiration. To maintain the homeostasis of the oral cavity, the human body has been equipped with several defense mechanisms. The structure of the oral mucous membrane with its high turnover rate and the capacity to secrete several antimicrobial peptides is itself an important defense mechanism to ward off infections and diseases that afflict the mouth [1]. The salivary glands and their secretions compositely termed as whole saliva is another important protective mechanism that aids in mastication, digestion, lubrication and phonation [2]. It is a noteworthy fact that saliva is a mixture of several defense molecules such as kallikerin, defensins, immunoglobulin A and immunoglobulin G which also exert antimicrobial and antiviral properties [3]. The gingival crevicular fluid termed the GCF is another secretion from the periodontium that is also involved in the host defense mechanism against many pathogens [4].

Despite the numerous physiological mechanisms that operate to ward off oral diseases as above mentioned, mankind is still afflicted by many oral diseases and conditions which are associated with significant morbidity. Dental caries and disease of the periodontium are the most common and globally prevalent oral conditions that are principally caused by pathogens present the dental plaque biofilm [5]. At this point it is to be mentioned that dental plaque is a biofilm that adheres on to the teeth and surfaces of restorations [6]. The accumulation of dental plaque is increased due to poor oral hygiene and improper brushing. The plaque biofilm is an ecological niche and houses several species of bacteria. Amongst these some bacterial species such as streptococci and actinomyces are implicated in causing dental caries which is a destruction of the dental hard tissues namely enamel and cementum [7]. Untreated dental caries can spread into the vital tissue of the teeth named pulp and can cause pulpitis and apical periodontitis which produce severe pain. Another biofilm induced disease of the oral tissues is periodontitis which is described as an inflammatory condition that causes destruction of the tooth supporting apparatus [8]. As a response to the microbial challenge mounted by the dental plaque biofilm, there is an inflammatory response that manifests in the gums/gingiva termed gingivitis if left untreated progresses to involve the deeper periodontal structures namely the cementum, periodontal ligament and alveolar bone causing mobility of the teeth, formation of pus pockets and abscesses. Both dental caries and diseases of the periodontium are curable conditions although irreversible in nature.

The oral cavity also bears the brunt of substance abuse other than bearing the burden and negative effects of poor oral hygiene. In this regard the use of cigarettes, cigars, beedi, pipe, hooka and smokeless forms of tobacco, paan, betel nut, betel leaf and alcohol pose significant threat to the oral tissues [9]. Since the above mentioned products have significant carcinogenic potential, they can induce oral premalignant diseases (OPMD) such as leukoplakia, erythroplakia, lichen planus and oral submucous fibrosis which have a significant malignant transformation rate and can finally transform to oral squamous cell carcinoma (OSCC)/oral cancer [10]. OSCC is one of the most common cancers world over and is also very prevalent in India where the use of tobacco and related products is very common [11].

At this juncture it is to be understood that dental caries, periodontal disease and oral cancer are important oral diseases that need attention, treatment and more importantly prevention which is always termed better than cure. With regard to the pathogenesis of the 3 conditions mentioned, it is to be understood that infection, inflammation and cytotoxicity play a major role. An equal role is played by oxidative stress which is defined as tissue damage caused by over production of free radicals and reactive oxygen species coupled with a depleted antioxidant status [12]. It has been proven beyond doubt that dental caries, diseases of the periodontium and oral cancer are free radical disorders. Hence for a holistic management of these oral diseases, an agent with multifaceted roles such as antimicrobial, anti-inflammatory and immune modulating, cytoprotective and antioxidant functions is needed. It is in this regard that melatonin deserves mention.

Melatonin chemically denoted as N-Acetyl-5 Methoxy tryptamine is an indole amine produced principally from the pineal gland during the dark phase of the day [13] although several other organs can synthesize melatonin [14–16]. In the oral cavity, the salivary glands [17] and the gum tissues/gingiva [18] are equipped with the capacity to synthesize melatonin. Melatonin levels are detectable in saliva and salivary melatonin has been described as one of the most important antioxidant systems in saliva [19]. Melatonin also has numerous other functions such as anti-inflammatory [20], immune modulating [21], cytoprotective [22], anticancer [23], bone sparing [24], antimicrobial [25] and antiviral [26] that make it a multifaceted molecule. Hence salivary melatonin could represent an important defense molecule protecting the oral cavity against dental caries, diseases of the periodontium and oral cancer. It is also known and documented that salivary melatonin levels are depleted in the above mentioned oral disease conditions due to enhanced oxidative stress that destroys melatonin [27, 28]. Hence the need for melatonin supplementation in the oral cavity arises to prevent and cure oral diseases.

It is in this regard that plant sources of melatonin need to be explored. At this juncture it is to be mentioned that melatonin is an evolutionarily conserved molecule that is found in almost all life forms including prokaryotes, eukaryotes and the plant kingdom [29]. And the molecule is chemically similar in all the life forms with the same biochemical pathway of synthesis. It is also been researched that diet derived melatonin can significantly impact humans and can be used as a method to enhance the levels of melatonin in the body [30]. It is in this regard that this chapter has been drafted to make the reader understand the herbal and plant derived sources of melatonin. The chapter further sheds light and provides recommendations on the use of plants rich in melatonin as a biochemopreventive measures for the management of oral diseases.

24.2 Melatonin: Chemistry, Evolution and Biosynthesis

Melatonin is chemically denoted as N-Acetyl-5 Methoxy tryptamine [13]. This indole amine molecule is known to be archaic and is also linked to the origin of life in the earth [31]. It is referred to as an evolutionarily conserved molecule that has been traced to the earliest prokaryotes that appeared on the planet. There is evidence for the presence and synthesis of melatonin in cyanobacteria and alpha-proteobacteria [32]. It is postulated that melatonin was synthesized and stored in the above organisms prior to a process termed to as endosymbiosis. After these bacteria were engulfed and phagocytosed by early prokaryotes, there occurred a transformation of the engulfed bacteria into organelles termed chloroplasts and mitochondria which till today retain the capacity to synthesize melatonin [33]. It is noteworthy that after significant organismal diversity, the indole amine melatonin has not changed structurally and still retains its chemistry. It is also significant to note that all organisms and living beings in the world in the plant, marine and animal kingdoms retain the capacity to synthesize melatonin. It also appears from the ubiquitous nature of melatonin, that it is a universal protector of cellular stress and is hence produced by all forms of life.

In the human system, melatonin is synthesized from the precursor amino acid tryptophan. The synthesis of melatonin in humans and animals occurs predominantly in the pineal gland during the dark phase of the day [13]. The pinealocytes, which are the resident cells of the pineal gland are endowed with the enzyme machinery for melatonin production. Starting with tryptophan, there are 4 significant steps in all organisms that mark the completion of melatonin synthesis. In this regard, Tryptophan is transformed to serotonin after decarboxylation and hydroxylation. The generation of serotonin is different in different taxa of living beings and differs in plants compared to higher vertebrates [33]. In plants, Tryptophan is converted to tryptamine by decarboxylation facilitated by tryptophan decarboxylase (TDC), followed by serotonin production mediated with the aid of tryptamine 5-hydroxylase (T5H) [33]. In animals, tryptophan is hydroxylated by tryptophan hydroxylase (TPH) into 5-hydroxytryptophan decarboxylation is further facilitated by aromatic amino acid decarboxylase (AADC) to produce serotonin. It is also noteworthy that in plants, the shikimic acid pathway operates to generate tryptophan required for melatonin biosynthesis [33].

Serotonin as demonstrated above is a pivotal molecule in the melatonin biosynthetic pathway. These steps that transform serotonin into melatonin involve serotonin *N*-acetyltransferase (ANAAT) and *N*-acetylserotonin *O*-methyltransferase (ASMT) also earlier termed as hydroxyindole-*O*-methyltransferase, HIOMT) [33]. ANAAT converts serotonin into *N*-acetylserotonin and HIOMT transforms N-Acetyl serotonin to produce melatonin. Alternatively, serotonin could be initially O-methylated into 5-methoxytryptamine through the action of HIOMT and following this could be acetylated by AANAT to generate melatonin. The classical and alternative pathways could operate in vertebrates, plants and microorganisms. Different homologs of AANAT and HIOMT have been observed in plants and animals, however, the final product namely melatonin has not been found to have any variation in structure among the various life forms again proving that melatonin is highly evolutionarily conserved as a biological molecule.

24.3 Functions of Melatonin in Living Beings

As earlier described, melatonin is an archaic molecule that is evolutionarily conserved. The pathways of melatonin biosynthesis have been described above. It is noteworthy that melatonin acts on its target tissues through both receptor mediated effects and receptor independent effects. Due to its small molecular weight and high lipophilicity [34], melatonin can cross all cellular layers and can easily penetrate the lipid bilayer of the target cells. The receptors for melatonin action are also many in subtypes [35]. The receptors known and researched so far are the G-protein coupled receptors MT1, MT2 and the other receptors related to melatonin namely Melatonin receptor type 1c, Quinone reductase 2 enzyme, RZR/RORα and GPR50: X-linked Melatonin-related Orphan receptor [35]. The presence of melatonin and its receptors in all the living beings on the surface of the earth explains its significance in maintaining homeostasis. The functions of melatonin in plants and animals have been illustrated in Figure 24.1. In plants, melatonin has been found to ubiquitously present and is synthesized. Melatonin levels in plants have been analyzed by various quantitative experiments and it has been found that the seeds and leaves of plants have high concentrations of melatonin, while the fruits have low concentrations. In plants, melatonin has been found to be a cell protector, regulates circadian rhythm and also has been found to control vegetative development [33].

In higher living beings such as mammals and humans, melatonin has been found to perform a spectrum of functions. The most important role of melatonin is its effects on regulating circadian rhythm in physiological state. Melatonin is a regulator of the biologic clock and promotes the setting of the sleep wake cycle, which is very important in regulating other physiological systems [36]. Melatonin is also found to demonstrate antioxidant activity against an array of free radicals and reactive oxygen species. In this connection, melatonin has been extensively investigated and results have demonstrated melatonin to act against a wide variety of radicals such as the lethal hydroxyl ion [37] and the superoxide anion [38]. Melatonin can also scavenge a wide variety of reactive nitrogen species [39]. An important feature of the interaction of melatonin with free radicals is the production of intermediate metabolites such as AMK and AFMK which are products with a short half-life generated from melatonin [40]. These intermediate metabolites are by themselves powerful radical scavengers. Hence it can be inferred that melatonin is different from the classical free radical scavengers which get destroyed upon interacting with free radicals. In the case of melatonin, a chain reaction is set up upon its interaction with a free radical molecule where several free radicals can be scavenged. The exponential quality and cascading nature of the reaction makes melatonin, natures best antioxidant gift to life. Melatonin also has a significant role in the mitochondrial respiratory chain. In fact, high concentrations of melatonin have been found in the cristae of the mitochondria where it scavenges free radicals generated from the respiratory chain and exerts antioxidant defense [41]. Melatonin also controls the synthesis and transcription of antioxidant systems such as the glutathione system and functions as a potent antioxidant [42].

With regard to the immune system, melatonin is known to have a cross talk with the immune system. In fact there is a concept of pineal immune cross talk with melatonin as the mediator [43]. In this regard, melatonin is known to act as a double edged sword with respect to the immune system. It is known to have both immunostimulatory effects [44] and immunosuppressive effects [44]. It can significantly control neutrophil chemotaxis,

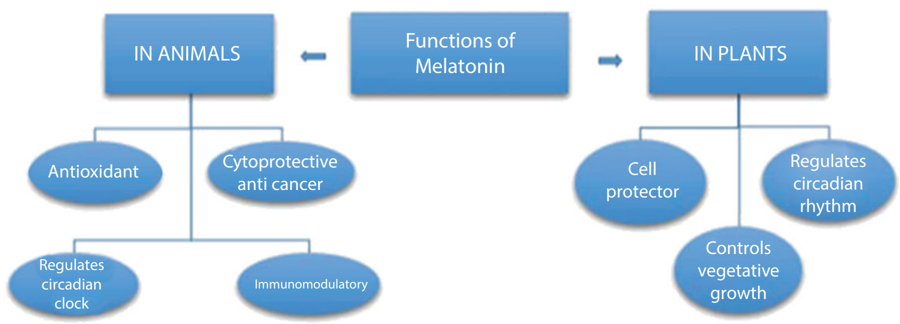

Figure 24.1 Functions of melatonin in plants and animals.

rolling and phagocytosis and also affects lymphocyte proliferation rates [44]. With regard to cytokine production, melatonin has an inhibitory effect on NF-kappa B and is found to be an anti-TNF alpha compound [45]. *In vitro* experiments and human assays have shown that melatonin levels correlate inversely with that of TNF alpha demonstrating an anti-cytokine role for melatonin. Hence it can be concluded that melatonin is an immunomodulator.

With regard to inflammation, melatonin has been proven to be an anti-inflammatory agent and a cytoprotective molecule [22]. It has been shown to protect the human body from various forms of toxicity. Notable among these are the role of melatonin in negating nickel [46] and copper toxicity [47] in animal models.

Melatonin is known to be an important molecule regulating bone health [48]. It has been described that melatonin improves the activity of osteoblasts and increases their proliferation and synthetic activity. It can also inhibit osteoclastogenesis and retards bone resorption in *in vitro* and animal models.

Melatonin has been known to be an antifibrotic molecule and has been known to prevent fibrosis and excessive matrix deposition in liver, kidney and myocardial fibrosis in animal models induced by carbon tetrachloride [49]. The antifibrotic effects of melatonin are mainly due to its anti-inflammatory, cytotoxic and antioxidant roles as earlier mentioned.

Apart from the above described, melatonin has been found to have significant anticancer effects and is also an inhibitor of cancer metastasis [50]. It has also been shown that melatonin is a significant inhibitor of the epithelial mesenchymal transition mechanism that operates in cancer spread and metastasis [51].

Considering all the above effects of melatonin, it appears that melatonin is one of the most multifaceted molecules in living organisms.

24.4 Melatonin and Oral Health

Considering all the above described effects of melatonin, it can be elucidated that melatonin could be a significant protector of oral health. However, oral diseases cause depletion of melatonin levels due to the destructive role played by infection, immune response and oxidative stress which all cause excessive melatonin sequestration and depletion thereby depriving the host of the beneficial effects of melatonin.

Melatonin levels have been assayed extensively in gingivitis and periodontitis which are termed diseases of the periodontium broadly. Gingivitis can be described as an inflammation of the gum tissues and is reversible while periodontitis is an irreversible condition characterized by deeper extension of inflammation from the gums/gingival tissues to the tooth supporting apparatus, namely the periodontal ligament, cementum and alveolar bone. Periodontitis is an irreversible condition and is clinically characterized by tooth mobility, gum bleeding, formation of abscesses and bad mouth odor. It is noteworthy that both gingivitis and periodontitis are caused by microbial infection from the dental plaque biofilm that accumulates on the tooth surfaces due to poor oral hygiene. Melatonin levels have been found to be lowered in saliva [52] and gingival crevicular fluid [53] samples of patients with gingivitis compared to their healthy counterparts. With regard to periodontitis, lowered melatonin levels have been demonstrated in saliva [54], gum tissue [55] and gingival crevicular fluid [56] samples compared to periodontally healthy subjects. Lowered melatonin levels in periodontal disease has been found to correlate with indices such as community periodontal index for treatment needs (CPITN) which indicate periodontal disease severity [57].

With regard to dental caries, also called dental decay, melatonin levels have been so far assayed only in 1 human study [58]. The results of this study have shown that melatonin levels are significantly lowered in saliva of caries active individuals compared to caries free individuals and is found to correlate inversely with the DMFT index (decayed, missing, filled teeth index) and also with malondialdehyde an oxidative stress marker.

Melatonin levels have also been found to be altered in patients with oral premalignant conditions such as lichen planus [59]. With regard to oral cancer, studies have focused on genetic polymorphisms of the melatonin receptors and have demonstrated abberations [60]. So far no study has been performed on salivary melatonin levels of oral cancer patients.

From the above data, it can be elucidated salivary melatonin levels depict the defense status in the mouth and are an indirect indicator of oral health.

24.5 Evidence for Use of Melatonin in Management of Oral Diseases

As described in the previous sections, the importance and significance of melatonin in maintaining homeostasis in the oral cavity has been highlighted. It has also been demonstrated that melatonin levels are depleted in oral disease in comparison with oral health. This makes it necessary for melatonin supplementation to boost oral health and defense.

Studies performed in this regard have mainly focused on the use of melatonin for management of periodontal disease, both topical application and systemic formulations of melatonin have been tried for the management of periodontitis as a host modulatory agent. It has been found that both systemic and topical forms of melatonin administered to humans with periodontitis can cause significant reduction in pocket depths, bleeding on probing and cause gain in attachment. Melatonin administration has also been found to reduce the levels of proinflammatory cytokines [61] and oxidative stress markers [62] in patients with periodontitis and also cause improvement in sleep patterns. Melatonin administration along with Vitamin C [63] found to have synergistic periodontal benefits. A recently performed systematic review and meta-analysis has highlighted the beneficial role of melatonin as a topical/systemic formulation for periodontitis management [64]. The systematic review highlights that more research needs to be performed in arriving at the standardized dose of melatonin as a perioceutical agent.

Melatonin has also been used in combination with bone grafts for attempting bone regeneration in periodontal, peri-implant defects and third molar extraction sockets. It has been found that the combination of melatonin with the bone graft increases regeneration scores and has a positive effect on bone formation, highlighting the osteopromotive effects of melatonin [65].

Another clinical condition where melatonin has been employed as a topical application is radiation induced oral mucositis. In this condition application of melatonin gel in post radiation patients suffering from oral mucositis has been found to provide pain relief and reduction of inflammatory scores [66].

24.6 Diet Derived Melatonin: Plants and Plant-Derived Food Rich in Melatonin

As earlier mentioned melatonin is ubiquitously present in all living beings on earth and hence becomes automatically a component of food and diet. There are some researchers who have pointed out that melatonin is a nutraceutical and also a vitamin due to its multi-faceted nature.

The melatonin content in plants and plant derived products is significant and is also termed phytomelatonin due to its nature of origin. As early as in 1995 there have been two published reports citing high melatonin content in plants and their parts [67, 68]. There are some species of plants and herbs that are rich in melatonin [69] and are described below in the Table 24.1.

Table 24.1 Plant foods that are rich in melatonin content.

S. no.	Plant/herb/seeds rich in melatonin
1.	Black pepper
2.	White mustard
3.	Turmeric
4.	Black mustard
5.	Goji berry
6.	Grapes
7.	Fennel
8.	Sunflower
9.	Almonds
10.	Radish
11.	Fenugreek
12.	Agati
13.	Alfalfa grass
14.	Elaichi/cardamom
15.	Flax seed
16.	Anise
17.	Coriander
18.	Celery

(*Continued*)

Table 24.1 Plant foods that are rich in melatonin content. (*Continued*)

S. no.	Plant/herb/seeds rich in melatonin
19.	Cherry
20.	Pomegranate
21.	Strawberry
22.	Corn
23.	Cucumber
24.	Oats
25.	Rice
26.	Wheatgerm
27.	Tomato

The herbs mentioned in the above table are common and an essential part of daily diet. These foods are consumed raw, semi cooked or fully cooked and would contain variable amounts of melatonin which would go into the human body in the form of food consumption.

It is also noteworthy that traditional herbal medicine also contains melatonin [70]. In this regard Thai medicine which is an indigenous medicine system in Thailand documented in a treatise called the Tumra Paetsart Sonkrau Chabub Anurak uses 7 herbs which are all rich in melatonin. The herbs documented in the ancient treatise are *Sesbania glandiflora* L., *Baccaurea ramiflora, Moringa oleifera* Lam., *Sesbania sesban* L. Merr., *Piper nigrum* L, *Momordica charantia* L., *Senna tora* L. Roxb. It has been documented that the extracts prepared as a concoction from the above listed herbs would be a tonic and aid sleep and regulation of circadian rhythm in humans.

In a similar fashion, melatonin levels have been assessed by chromatographic assay techniques in Chinese herbal medicine. It is to be mentioned that this juncture that Chinese herbal medicine uses about 100 herbs out of which 64 herbs are rich in melatonin [71]. Herbal infusion teas containing Chinese herbs have also been shown to contain high levels of detectable melatonin especially green tea and chamomile tea [72].

A study from Egypt on traditional Egyptian food has documented that the 3 most important substances in animal physiology that control the human body in homeostasis are melatonin, serotonin and tryptamine. The study documented high melatonin levels in some commonly consumed vegetables and fruits in Egyptian cuisine such as unripe banana, corn, ginger, barely seeds and rice [73]. The study also demonstrated detectable melatonin levels in strawberry and pomegranate and absence of the indoleamine in potato.

Another study on Mediterranean diets has demonstrated the consumption of wine, olive oil, tomato, grapes and beer in this region and has documented significantly high levels of melatonin in these foods [74].

Considering all the above evidences, it appears that melatonin is an important component of food and traditional medicine systems. The next question that needs to be answered is if consumption of melatonin from food could increase melatonin levels in the human system. To answer this question, there are studies performed on humans which have shown increased bioavailability of melatonin in the plasma after consumption of melatonin rich foods such as wheat, grains and grapes [75, 76]. The study also showed that consumption of beer enhances melatonin levels in blood as evidenced by increased excretion of melatonin metabolites in urine [77].

Another important nutritional fact is that the availability of some vitamins and minerals such as magnesium, folate, zinc and vitamin B6 derived from phytoconstituents is required in the human body to maintain significant melatonin levels [78–80].

24.7 Hypothesis Promoting Use of Phytomelatonin for Prevention of Oral Diseases

From the above sections, it could be understood that melatonin is a beneficial molecule to maintain oral and systemic health. Melatonin is multifaceted and is present in all living forms in this universe and can be diet derived as evidenced in this chapter. It is also to be understood that diet is an important form of enhancing the plasma levels of melatonin.

With regard to prevention and management of oral diseases diet has been emphasized to play a central role. Diet is a vehicle to deliver nutrients, vitamins, minerals and trace elements to the human body for maintenance of homeostasis. There are studies on dental caries and periodontal disease that have shown the relevance of diet for disease prevention. While consumption of refined food, sugars and sticky food has been linked to dental caries progression [81], the intake of green tea [82], Chinese herbs [83] and certain phytoconstituents are known to prevent dental caries. In a similar manner periodontal disease could also be prevented by the intake of diet derived phytochemicals as demonstrated by animal and human studies [82, 84, 85]. The same is the case of oral cancer where diet plays a vital role in disease occurrence, prevention and progression [86]. This area of medicine using herbs and herb derived phytoconstituents for disease prevention is termed as biochemoprevention [87].

In the context of this chapter, it has been reviewed and found that the intake of the above listed melatonin rich herbs have also been found be linked to low incidence of dental caries, periodontal disease and oral cancer as depicted in Figure 24.2. Turmeric containing tooth pastes have been documented to prevent dental caries and periodontal disease [88]. Grape extracts have been found to reduce the incidence of dental caries [89]. Grape derived products have been linked to low incidence of dental caries and periodontal disease [90]. Cardamom extracts have also been shown to reduce occurrence of periodontal infections [91]. Pomegranate extract containing mouthwashes have been proven to possess antiplaque and periodontitis preventive qualities [92, 93]. There is ample evidence to show that fenugreek extracts containing gels can prevent and aid in management of periodontal disease [94, 95].

From all the evidences available in published literature, it appears that melatonin rich herbs, fruits and vegetables have a positive impact on oral health. Even though there is data

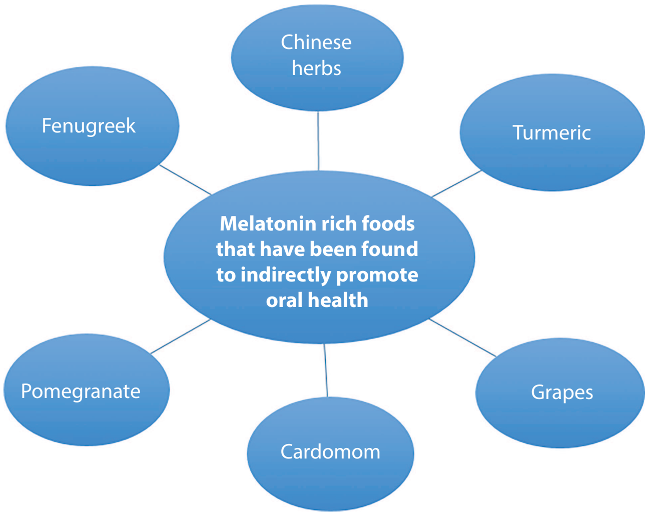

Figure 24.2 Melatonin rash herbs that have been found to promote oral health.

supporting the use of melatonin in systemic or topical formulation for management of oral diseases, there is no hypothesis supporting the inclusion of melatonin rich food in daily diet, which could promote not only oral health but also systemic health. the earlier sections have highlighted the multifaceted nature of melatonin as a promoter of the biological clock, anti-inflammatory, cytoprotective, immunomodulatory and anticancer molecule in addition to being one of the most potent antioxidants. At this juncture it is also to be reiterated as earlier mentioned that melatonin is a promoter of oral health and can play a key role in the prevention and progression of dental caries, periodontal disease and oral cancer. It has also been demonstrated that consumption of melatonin rich diets could elevate plasma levels of melatonin. We hence hypothesize that the regular inclusion of melatonin rich foods could be done in daily diet to improve overall oral and systemic health. Since diet is the most holistic way of consuming nutrients with least side effects, we believe that melatonin delivered through diet would be the best form to exert its health benefits.

More longitudinal clinical studies on humans would be required to demonstrate the effects of melatonin rich diets on oral health in terms of reduced progression of dental caries, periodontal disease and oral premalignant lesions. If fruitful data is obtained from these studies it would be worthwhile including melatonin rich foods in the diet plan of patients of all age groups to exploit the systemic and oral benefits of melatonin.

24.8 Conclusion

Melatonin also termed N-Acetyl-5 hydroxy tryptamine is an indole amine found ubiquitously in all living beings. This molecule plays a potent role as an antioxidant, anti-inflammatory, cytoprotective and immunomodulatory agent and found to be a potent regulator of circadian rhythm. Melatonin has been found to be depleted in oral diseases such as dental caries, periodontal disease and oral cancer. Melatonin administration through systemic and topical formulations has been shown to be effective in treatment of oral diseases such as periodontitis. Since melatonin is ubiquitously present as earlier mentioned, food is also believed to be a source of melatonin and certain fruits, vegetables, cereals and herbs are known to be melatonin rich. Since consumption of melatonin rich food can raise/elevate blood melatonin levels, we propose the use of these foods in prevention and worsening of oral diseases like dental caries, periodontal disease and oral cancer. We propose the use of diet derived melatonin as a modality of improving oral and overall systemic health of a patient taking into account the multifaceted nature of melatonin.

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