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Review Article

Biological Activities and Traditional Use of *Hyptis suaveolens* in Human and Veterinary Medicine: A Review

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ABSTRACT

Hyptis suaveolens (*H. suaveolens*), known as Gros baume or sweet-smelling Hyptis, is an invasive plant from tropical regions widely used to manage human and animal ailments, such as bacterial, viral, and parasitic diseases. This study aimed to synthesize scientific research works on the use of this medicinal plant in the traditional pharmacopeia, as well as the biological and pharmacological activities already recognized in the literature. Information for this synthesis was collected from physical (libraries and documentation centers of universities in Benin) and reliable scientific databases, such as PubMed, Google Scholar, Scopus, and Web of Science, which were queried based on the keywords related to *H. suaveolens*. This plant contains secondary metabolites in its aerial parts, such as leaves, and stems, which are rich in essential oils. From leaves to roots, all parts of this plant are of interest to both humans and animals to treat various pathologies. The most frequently cited diseases include asthma, panariasis, jaundice, hyperthermia, indigestion, stomach pains, nausea, colds, gall bladder infections, breast abscesses, hemorrhoids, oral-anal candidiasis, edemas, cramps, and skin infections. The various aqueous and ethanolic extracts are evaluated by researchers and the biological activities are indicated in the literature. Those activities include the antibacterial, antifungal, larvicidal, antioxidant, anticholinesterase, insect repellent, and insecticidal effects. However, no toxicity resulting from the use of this plant has yet been reported in the literature. Research on *H. suaveolens* toxicity must be continued to gain a comprehensive understanding of its application in human and livestock health. This literature review allows the virtues and risks related to the traditional use of *H. suaveolens* in human and animal pharmacopeia. The various potentialities of this plant provide a lever for exploring its antiviral effects in traditional veterinary medicine in general.

1. Introduction

Medicinal plants have been used by mankind since ancient times. However, these practices were neglected with the advent of synthetic chemical processes and the creation of so-called allopathic medicine[1]. Today, the multiple public health risks associated with the presence of residues in the food chain or antibiotic resistance have encouraged the emergence of ethnomedicine[2]. With this in mind, the WHO has urged developing countries to give greater prominence to their traditional pharmacopeia, given that costly modern medicine benefits affluent countries[3]. The utilization of herbal drugs in human medicine is on the rise[1], a trend observed not only in general human

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healthcare but also in veterinary medicine[4,5]. This growing adoption of herbal remedies extends to over 80% of the African population at large and is particularly notable in countries like Benin[6,7]. This rise can be due to the availability of plant resources and the relatively affordable cost of medicinal recipes. The efficiency of certain local recipes in the treatment of several pathologies (infections and parasitic disease), with low side effects for most of them, make them more interesting than synthetic chemical molecules[8,9].

In Africa, and particularly in Benin, several studies have highlighted the value of using medicinal plants by livestock farmers to treat their animals[10-16]. Thus, the research carried out by Toyang et al.[17] in sub-Saharan Africa provides an overview of ethnomedicinal treatments for several animal diseases[10]. One of the commonly used plant resources is *Hyptis suaveolens* (*H. suaveolens*), which has been the subject of many biological, phytochemical, and pharmacological studies, as well as its multiple uses in human and animal nutrition. Some authors have justified that *H. suaveolens* possesses antifungal, anti-infectious, antiparasitic, insecticidal, and insect-repellent activities[10,18-21].

Hyptis suaveolens is a highly odorous plant from the Lamiaceae family, greatly reducing biodiversity and pasture productivity[2 2]. The essential parts used are the leaves, stems, and roots[11], whose analysis of chemical compounds reveals the presence of alkaloids, gallic and catechin tannins, anthocyanins, quinone derivatives, triterpenoids, steroids, mucilages, and reduced compounds[12]. The presence of these secondary metabolites in this medicinal plant gives it antiplasmodic, antioxidant, antibacterial, antifungal, antidiabetic, antirheumatic, antisuporific, anti-inflammatory, and antiseptic properties in burns and multiple skin complications on both human and animal[23]. Although the decoction of *H. suaveolens* roots has a high urosolic acid content (a natural inhibitor of HIV integration)[24], antiviral properties of this plant have been reported in the scientific literature.

The present work summarizes studies carried out on *H. suaveolens* (L.) Poit, focusing on aspects relating to its biological, pharmacological, and phytochemical use in traditional human and veterinary medicine. This study opens up the prospect of assessing the antiviral effects of plant extracts on human/animal pathologies in general.

2. Literature

This bibliographic synthesis was based on a literature review that took into account both physical and digital documents relating to *H. suaveolens.* Physical documents were books, doctoral theses, dissertations, newspaper articles, educational magazines, and conference reports available and collected in the libraries and documentation centers of certain Faculties and Schools of the Universities of Abomey-Calavi and Parakou in Benin. The digital documents searched for were obtained by direct contact with the authors and/or via the Internet with search engines such as PubMed, Google Scholar, and Web of Science, assisted by metadata storage systems (Research Gate, Springer Online, Scopus, and Science Direct).

Scientific databases were queried on the basis of keywords relating to *H. suaveolens* and related to "traditional uses", "human medicine", "veterinary medicine", "phytochemical composition", "biological properties", "pharmacological activities" and "toxic effects". This made it possible to download many scientific documents selected based on their titles, abstracts, and keywords. A total count of all the documents downloaded for this synthesis was made in a database (Zotéro), followed by classification according to title. After an analysis, the documents were compiled and selected to retain only those relating to the theme "Synthesis of the biological activities and use of *H. suaveolens* in traditional human and veterinary medicine". 103 publications were recorded in all. After selection, 24 invalid publications (works unrelated to the theme, subject out of context and duplicate documents) were excluded. After analysis and categorization, 79 scientific publications were retained, including 55 original articles, 9 doctoral theses, 8 books, 4 technical reports, and 3 scientific papers. This literature search could determine the virtues and properties of the plant that is the subject of this synthesis.

3. Curve of literature publication

Figure 1 shows the curve of publications in relation to

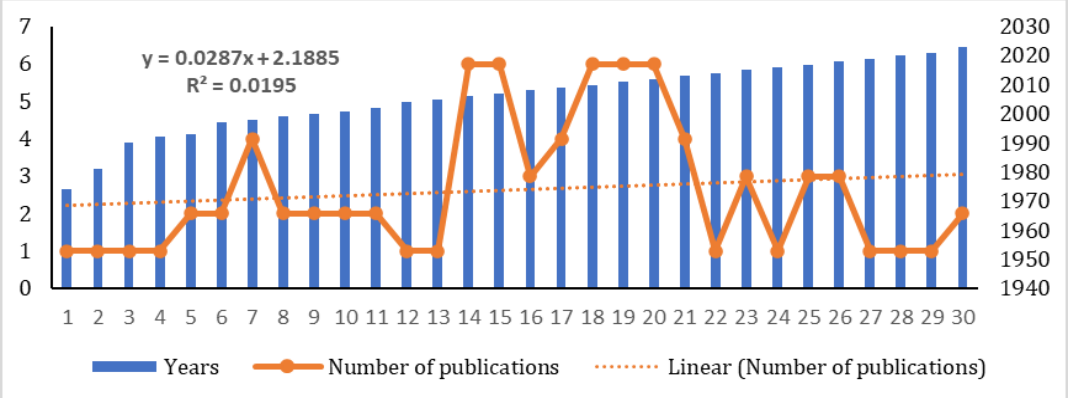

Figure 1. Number of publications on *Hyptis suaveolens* from 1974 to 2023

their years of notification. The year and the number of publications made on *H. suaveolens* made it possible to obtain an ascending linear regression indicating the evolution of research involving the plant species cited in this bibliographic synthesis. Y corresponds to the number of publications. R^2 is the coefficient of determination that makes measuring the quality of linear adjustment between X and Y possible.

4. Botanical description and geographical distribution

Hyptis suaveolens, also known as *Ballota suaveolens, is a* shrubby plant in the Lamiaceae or Labiatae family, comprising more than 250 genera and nearly 7,000 species spread across the globe, but particularly well represented from the Mediterranean basin to Central Asia[25]. The *Hyptis* genus is subdivided into three tropical species, including *Hyptis spicigera* Lam, *Hyptis lanceolata* Poiret, and *H. suaveolens* (L.) Poit. Widespread in tropical Asia and Africa, *H. suaveolens* originated in tropical America and is now found throughout the world's tropical regions[26]. It is a terrestrial, aromatic annual herb growing up to two meters high. Leaves are simple, entire, petiolate, opposite, and pubescent on both sides. Flowers are purplish in color, hermaphroditic, sessile, and grouped in axillary glomerules. The fruit is a tetrakene containing four seeds clustered at the bottom of the calyx. Field studies have revealed that *H. suaveolens* is a sporadic weed in rice fields[26,27]. It grows in fallow fields, pastures, undeveloped plots, and along roadsides. Work on production techniques has shown that this plant (Figure 2) grows very easily in West Africa when the direct seeding technique is used[13,28-30].

5. Chemical composition

Phytochemical screening of *H. suaveolens* leaves has revealed the presence of all the following families of secondary metabolites, including carbohydrates, alkaloids, simple sugars, steroids, terpenoids, tannins, flavonoids, anthraquinones, phenols, which account for over 13% of dry leaves mass[12,31-33]. However, this does not reject the results obtained by Nantitanon et al.[20], revealing that the geographical environment is a factor influencing the phytochemical composition of a plant species. *Hyptis suaveolens* leaves contain essential oils[31] with menthol, limonenes, and sesquiterpenes[34], which have numerous pharmacological and biological properties[35]. Several volatile compounds contained in the leaves of this plant (β-caryophyllene, bergamotene, terpinolene, humulene, sabinene, and limonene) have been reported for the most part as insect repellents and insecticides[36,37]. Several authors cited by Koné[38] have justified that the plant contains a yellow-green etheric oil with hydrocyanic acid, in its roots, barks, and leaves. A phytotoxic substance called suaveolic acid (14α-hydroxy-13β-abiet-8-en-18-oic) has been isolated from the methanolic extract of the whole plant of *H. suaveolens*[39].

Figure 2. *Hyptis suaveolens* (L.) Poit, Source: Phoyographie (Sèdégan 2023)

Per 100 g of powder, the yields of dry extracts of chloroformic, ethanolic, and aqueous in *H. suaveolens* leaves were 1.14%, 2.26%, and 4.43%, respectively[19]. The highest yield was obtained with aqueous extraction. These chloroformic, ethanolic extracts have a blackish pasty appearance, while the aqueous extract presents a brown-green gummy appearance.

6. Traditional use of *Hyptis suaveolens*

In Africa and tropical zones, *H. suaveolens* is widely used in traditional pharmacopeia to treat a variety of pathologies, the most frequently cited of which are asthma, panariasis, jaundice, hyperthermia, indigestion, stomach pains, nausea, colds, gall bladder infections, breast abscesses, hemorrhoids, candidiasis of the mouth and throat, indigestion, stomach pain, nausea, colds, gallbladder infections, breast abscesses, hemorrhoids, oral-anal candidiasis, edema, cramps, and skin infections[29,37,40-42]. In Benin, an ethnobotanical survey revealed that *H. suaveolens* is served at 6.1% by market herbalists among plants used to treat infections and 13% among traditional plant users in humans[43-46]. These results align with those of Kouchadé et al.[19] indicating that *H. suaveolens* is excellently used in the management of candidiasis and other childhood illnesses and infections. The decoction of its roots is used as an aperitif[13].

In Côte d'Ivoire and Senegal, alternative pest control methods using aqueous extracts of *H. suaveolens* have been developed[47,48] . The inflorescences are introduced under mattresses as insecticides, and the smoke released by burning the whole plant is an excellent insect repellent[48,49]. The *H. suaveolens* extracts are also used in the preparation of mosquitos (mosquito-smoking sticks)[50]. In veterinary ethnomedicine, *H. suaveolens is* also cited among the pharmacological plants recognized and used by livestock breeders in Africa[51]. In Benin, it has been observed that the plant is also used by livestock farmers as a healthy food for rodents (rabbits and aulacodes), although its use in animal medicine has received very little attention in the scientific

literature.

7. Biological activities of *Hyptis suaveolens*

The antibacterial and antifungal activities of the essential oils and leaf extracts of *H. suaveolens were* evaluated on a number of microorganisms in order to justify the plant's traditional use. Antimicrobial tests were carried out on dry extracts (aqueous, ethanolic, and chloroformic) and essential oils of the plant on *Staphylococcus (St.) aureus, Pseudomonas aeruginosa, Escherichia (E.) coli, Pasteurella multocida, Erysipelothrix rhusiopathia, Actinomyces pyogenese, Streptococcus suis, Salmonella spp., Candida (C.) albicans, Trichophyton (T.) mentagrophytes*[19,20]. The results have revealed that *H. suaveolens* extracts have more antifungal than antibacterial properties.

7.1. Antibacterial activity

The *H. suaveolens* extracts have a strong inhibitory effect on the growth of the bacterial germs studied at a concentration of 20 $mgml^{-1}$ except for *St. aureus*, which remained only slightly insensitive to certain extracts[19], which confirms the plant's antibacterial potential. Meanwhile, the aqueous extract of *H. suaveolens* proved more active on *E. coli, St. aureus,* and *C. albicans,* with zero action on *Salmonella spp.* Agban et al.[19] and Pachkore et al.[46] showed that the ethanolic extract was more active than the aqueous extract against the growth of *E. coli*. Chitra et al.[49] found that petroleum ether, chloroform-water, and ethanolic extracts of *H. suaveolens* leaves had strong antibacterial activity against *E. coli*[49]. In contrast, essential oil from the aerial part of *H. suaveolens* has a weak inhibitory effect on *E. coli* growth[20]. In addition, essential oils from the leaves and ethanolic, etheric and chloroform extracts from the leaves, stems and roots of *Hyptis suaveolens* induced inhibitory effects on the growth of *St. aureus*[10,20,49].

7.2. Antifungal activity

The chloroform extract completely inhibited the growth of *C. albicans*, whose minimal inhibition concentration was determined to be 1.25 $mgml^{-1}$ [19]. These antifungal tests, which were carried out using the principle of dilution in liquid medium coupled with spreading on agar medium[19,50] confirm the findings of Kouchadé et al.[12], which stipulate that *H. suaveolens* is more widely used in the management of candidiasis.

Rojas et al.[51] had already reported the antifungal effect of *H. suaveolens* extracts on *C. albicans*, and details of the inhibitory effects on *C. albicans* growth of methanolic, ethanolic, chloroformic, etheric, and aqueous extracts of *H. suaveolens* were shown by Agban et al.[19], Pachkore et al.[48] and Mbatchou et al.[52] in their studies. In addition, the antifungal activity of the essential oil of the aerial parts of *H. suaveolens has been* proven on the dermatophytes *T. mentagrophytes*[20]. It is clear from the above that *H. suaveolens* is a medicinal plant with antifungal and antibacterial properties that can be exploited.

7.3. Larvicidal (anti-plasmodial) activity

The most widely used method for identifying larvicidal activity of *H. suaveolens* is inspired by the sensitivity test technique standardized by the WHO and adopted for testing larval sensitivity to the drugs used[2]. Generally, non-organic extracts have a higher larvicidal activity than organic extracts. Thus, larvicidal tests carried out with aqueous extracts of 10 plants from the Malian flora, including *H. suaveolens,* gave no mortality of *Anopheles gambiae* larvae[53]. This confirms the low mortality obtained by Koné[35] with organic extracts after 24 hours of exposure despite an increase in concentration to 1,000 µg/mL. In contrast, Aouinty et al.[54] obtained 100% mortality of *Culex pipiens* larvae in Morocco *at* a concentration of 1% with aqueous extracts of *Ricinus communis*. This suggests that a plant's lack of larvicidal activity could be justified by its nature and the type of larva.

Koné[35] observed total larvicidal activity with the methanolic and ethereal extracts of *H. suaveolens* at 1,000 µg/mL after 24 hours, as well as with the dichloromethane extract, which showed almost total mortality of 97% on *Anopheles gambiae* larvae at the same concentration. The larvicidal activity of *H. suaveolens* varies according to the type of extract, although it appears that alcoholic extracts are highly active on larvae, justifying the results of numerous research studies[21,53,55,56]. However, a more rapid larvicidal activity on *Anopheles gambiae*, compared with other extracts, was observed with petroleum ether extract, with 100% mortality in one hour[38]. Similarly, comparing the lethal concentration CL_{50} of several medicinal plants, Koné[38] observed that *H. suaveolens* was even more effective on the larvae, before suggesting that it would be important to study this potentially larvicidal (antiplasmodial) medicinal plant further.

7.4. Anticholinesterase activity

The substances responsible for anticholinesterase activity are present in low quantities in *H. suaveolens* decocts, or are absent from the aerial parts of the plant[35]. On the other hand, the apolar extract of the plant has demonstrated very good anticholinesterase activity, which decreases with the polarity of the extract[38]. Greater anticholinesterase activity is observed in extracts that are more apolar. However, Koné[38], using the colorimetric method based on the Ellman test, showed in his study that ethereal, dichloromethane and methanolic extracts of *H.suaveolens* proved no remarkable anticholinesterase activity.

In Nigeria, Peter et al.[57] used Ellman spectrophotometry to demonstrate the anticholinesterase activity of crude methanolic extracts of medicinal plants, with alkaloids as the responsible substances. Similarly, Ferreira et al.[58] cited alkaloids, terpenes, glycosides, and coumarins as chemical compounds with anticholinesterase properties, Notably, *H.*

suaveolens was found to contain these compounds[12,31] . In the same study, plants belonging to *Laminaceae* family (*H. suaveolens)* were found to have anticholinesterase properties[58]. All these data justify the acetylcholinesterase-inhibiting activity of the medicinal plant *H. suaveolens.*

7.5. Antioxidant activity

Antioxidants prevent cell damage caused by free radicals normally released during normal metabolism[38]. They protect the body against cancer and other cardiovascular diseases[59]. In Mali, Koné[38] showed that aqueous and methanolic extracts of *H. suaveolens* have reduced the free radical of the 1,1diphenyl-2-picrylhydrazyl (DPPH) with very marked antioxidant activity, the results of which are presented as yellow spots on a violet-background plate. The antioxidant action of these different extracts could be explained by their richness in polyphenolic substances, tannins, coumarins, flavonoids and saponosides. In line with the answers given by Bruneton and Cavin[60,61], justifying the above-mentioned chemical compounds as potential antioxidants[62], quoted by Koné[38], justifies the antioxidant activity of *H. suaveolens* as a substance rich in flavonoids (antioxidant substances active in maintaining blood circulation, as they contribute to increasing the production of nitric oxide by blood platelets, which limits clot formation by preventing platelets from clumping together).

7.6. Insect repellent and insecticide

Hyptis suaveolens is a plant species with both insecticidal and repellent properties[63-65], for the control of insect pests of field crops. It is a massively cultivated plant in regions of Africa where nuisance mosquitoes, vectors of disease, are rife[18]. The aerial parts of the plant are used as a safe mosquito repellent, as they show no human toxicity[18,66]. A study by Azeez[65] indicated that *H. suaveolens* powder causes significant mortality (100%) in invertebrates (*Callosobruchus maculatus)* after 7 days of treatment.

In Senegal, *H. suaveolens* inflorescences are introduced under mattresses to repel adult mosquitoes. Similarly, Sane[44] has shown that the drop in the number of *H. armigera* caterpillars in cotton plots treated with aqueous extracts of *H. suaveolens* is due to the plant's repellent and insecticidal properties*.* The repellent action is also due to the volatile substances emitted by the plant, which contains essential oils with contact toxicity and a positive repellent effect at low doses[68]. These essential oils contain active compounds such as geraniol, 1,8 cineole, linalool, myrcene, limonene, and phellandrene, which possess insecticidal properties[69]. This was confirmed by Conti et al.[70] reporting that *H. suaveolens* essential oils have a repellent activity on *Sitophilus granarius* adults due to the presence of molecules such as 1,8 cineole, carvacrol, α-pinene and β-pinene. Guèye et al.[71] were able to preserve corn cobs for 7 months without insect attack by a system alternating layers of corn with *H. spicigera* leaves, then it could be asserted that *H. suaveolens* possessed the same protective effects on cereals against harmful insects. Similarly, an extract of *H. suaveolens* has been shown to effectively control maize pests, notably *Mussidia nigrivenella* Ragonot[72-74]. The work of Kossou et al.[63] demonstrated that the aqueous extract of fresh *H. suaveolens* leaves could exert a lethal action on adults and larvae. This effect was also confirmed by Tano et al.[43] and Tounou et al.[75], who reported the efficacy of aqueous extract of *H. suaveolens* leaves on the caterpillars of *Hellula undalis*, and *Maruca vitrata*, pests of the cabbage crop.

8. Other biological activities

Several other activities of *H. suaveolens,* linking anti-inflammatory, antinociceptive, antiulcer, antidiabetic, antirheumatic, antisuporific, antiseptic, anticatarrhal, cutaneous antiparasitic and cytotoxicity properties have been reported in the literatures[23,76-78]. In addition, aqueous extracts of *H. suaveolens* leaves have been shown to be effective against green pepper mottle virus and its vector (*aphids)*[77] , and the decoction of its roots is reputed to contain urosolic acid, a natural inhibitor of HIV integration[24].

9. Prospect for usage and issues

In Africa as a tropical zone, *H. suaveolens* is a medicinal plant widely used in traditional pharmacopoeia to treat a variety of contagious and non-contagious pathologies, both infectious and parasitic[14,29,37,40-42,]. In Benin, Kouchadé et al.[18] have shown that *H. suaveolens* is excellently used in the treatment of candidiasis and other childhood illnesses. The decoction of its roots is also used as an aperitif[24]. In traditional veterinary pharmacopoeia, *H. suaveolens* has been little cited among the plants for pharmacological use recognized and used by livestock farmers in Africa[47]. Nevertheless, in southern Benin, Sèdégan et al.[15] reported that traditional poultry farmers had identified and used *H. suaveolens* leaves and stems in the treatment of fowl pox, with mixed results. These poor results could be explained by a lack of knowledge of the plant's gallic forms of use and consequently of its therapeutic doses. Studies on the use of medicinal plants need to be broadened to include phytochemical, pharmacological[12] and pharmaco-toxicological aspects for better rationalization of administration doses[16]. Hence, this bibliographic synthesis is important because it will better understand the chemical compounds of *H. suaveolens*, its various biological and pharmacological activities, and its oral toxicity. As a result, the practice of phytotherapy and aromatherapy is growing in human and veterinary medicine[1]. Involvement of this bibliographic synthesis today, a new boom in natural medicine has become a reality, linked to the development of organic farming and, above all, the search for new anti-infective molecules as alternatives to synthetic antibiotics to combat the emergence of resistance induced by their misuse[79]. These practices are increasingly sought-after, despite the still small number of scientific studies carried out on the subject.

However, this bibliographic synthesis provides a broad knowledge of the therapeutic use of *H. suaveolens* in traditional medicine.

10. Conclusion

Hyptis suaveolens is a medicinal plant widely used in the traditional human and veterinary pharmacopeia. All parts of the plant (leaves, stems, and roots) are used for a variety of purposes. Phytochemical tests and biological effects have been extensively discussed by several authors. The plant has been the subject of several studies, the results of which have had a positive impact on its pharmacological character through its antioxidant, antibacterial, skin antiparasitic, antifungal, anti-inflammatory, anticholinesterase, and larvicidal activities. Its insecticidal and insect-repellent effects rival many synthetic chemical insecticides on the market. However, the antiviral effects of this species in relation to veterinary medicine have not yet been addressed. In view of these scientifically proven therapeutic virtues, *in vivo* and *in vitro* testing of the various extracts of *H. suaveolens* must continue with a view to manufacturing phytomedicines from this plant. The results of work carried out on the traditional use of *H. suaveolens,* as well as the biological and pharmacological activities justified in favor of this medicinal plant, should provide relief to those involved in traditional medicine.

Declarations

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

Bienvenue Sèdégan, Yao Akpo, Cyrille Boko, and Guy Apollinaire Mensah developed the design plan for this literature review. All authors participated in the collection of data. Bienvenue Sèdégan drafted the article, assisted by Christhophe Iwaka and Alassan Assani Seidou. The critical observations of the article and its final approval were provided by Yao Akpo, Cyrille Boko, Eloi Attakpa, Guy Apollinaire Mensah, and Ibrahim Alkoiret. All authors have read and approved the final manuscript.

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All data are included within the article.

Ethical considerations

Neither this literature review nor any part of the manuscript has been published in any form elsewhere. All authors are in agreement with the content of the manuscript and its original submission to the journal.

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