RESEARCH PAPER

Larvicidal Activity Of Marine Macroalgae: A Comprehensive Review

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ABSTRACT
The problem of diseases transmitted by mosquitoes is a serious issue in global health, causing high mortality rates and economic losses. Although chemical insecticides have long been the mainstay in vector control, their efficacy has been diminishing because of the development of resistance in insects and increasing concerns about their toxicity to the environment and human health.Thisreview examines the use of marine macroalgae (seaweeds) as a sustainable, biodegradable, and environmentally friendly alternative for the control of mosquito larvae. Macroalgae in the three main categories: Chlorophyta (green algae), Phaeophyceae (brown algae), and Rhodophyta (red algae), have a vast secondary metabolite profile that includes phenolics, terpenoids, alkaloids, and sulphated polysaccharides. These compounds display toxicity to major mosquito vectors such as Aedes aegypti, Anopheles stephensi, and Culex quinquefasciatus through several modes of action, Physiological Disruption. The extracts directly affect the larval midgut epithelium, causing cell lysis and tissue disruption.Biochemical Interference of the bioactive compounds interfere with the activity of key enzymes such as acetylcholinesterase and cause oxidative stress through the overproduction of reactive oxygen species. The Growth Regulation of certain metabolites can affect hormonal balances, cause an extension of the larval stage or prevent successful pupation and emergence of the adult.Studies have shown high larvicidal activity. In addition to vector control, macroalgae-derived compounds have been identified as promising broad-spectrum antiviral drugs against pathogens such as SARS-CoV-2 and the influenza virus. The conceptcan provide a sustainable and multi-faceted solution for the control of mosquito-borne diseases with minimal ecological impact by using Marine Macroalgae.

Key words: Marine macroalgae, Larvicidal activity, Vector control, Mosquito-borne diseases, Secondary metabolites, Insecticide resistance, Enzyme inhibition, Midgut disruption, Anti-viral drugs.

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BACKGROUND

The mosquito-borne diseases have created a substantial health challenge for many countries of the world and continue to pose a severe challenge to public health services globally. The significant number of deaths and diseases these mosquito-borne infections claim each year make these diseases endemic[1]. The use of data collected and analysed from the Global Burden of Disease Study of 2021 indicates clearly and conclusively that malaria and other mosquito-borne infections still pose a wide threat to human health and claim significant numbers of lives and lower health standards around the world. The increasing number of mosquito-borne infections and deaths claimed by diseases like dengue fever over the past three decades pose a challenge of increased health and public concern as it is reported to result from influences like urbanization and increased travel between countries [2]. The mosquito-borne infections and diseases not only lower health standards but also pose a significant challenge of losses and reductions in national and public socioeconomics as far as endemic countries are concerned. The nature of this public health problem and challenge necessitates effective and innovative means of vector control using naturally derived mosquito killers like macroalgae seasoned into anti-mosquito agents[3].Synthetics have played a very important role throughout the history of modern-day mosquito control efforts; but with widespread use of these larvicides over a period of several decades, many limitations have been

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identified on a scientific and operational level[4]. The single biggest limiting factor facing vector control efforts has been the issue of resistance development within populations of disease-transmitting mosquitoes.

Widespread use of traditional insecticides like organophosphates, pyrethroids, and carbamates forces populations of disease-transmitting pests to become resistant to commonly used larvicides,[5] thus creating a reduction in the efficacy of traditional controls and forcing control efforts around the world to use larger application rates. This has been demonstrated with populations of various vector species.Aside from the issue of resistance evolution to these control tactics, the toxicity to the environment and the non-target species have also been major concerns. For example, the widely used chemical larvicides such as tempos and diflubenzuron have been proven to have high risks to the ecotoxicity of the species Daphnia Magna in waters at lower concentrations than the recommended field rates[6]. They could be detrimental to the freshwater biota.

Moreover, the groups of insecticides in wide application in the control of vectors have been noted as detrimental to some non-target species such as insects, aquatic organisms, as well as vertebrate species[7].In terms of other characteristics, human health and government regulation are part of this. Some larvicides have short- and/or long-term effects on non-target species such as mammals and humans, leading to various government decrees banning or limiting their use. For instance, organophosphate derivatives have health ramifications related to nervous system toxicity when highly exposed[8].In other cases, chemicals have bioaccumulative properties leading to unsafe buildup in tissues and soils.Operational/field performance constraints also work against the efficacious use of synthetic larvicides. Control measures tend to be heavily dependent upon particular environmental factors such as water type, temperature, and the amount of organic matter present. In addition to this, the number of approved active ingredients at the disposal of those controlling these vectors is also small. Coupled with the emergence of resistance strains, this fuels a reliance on fewer toxic agents [9].

The scientific and practical considerations outlined above also emphasize pressure on seeking alternative approaches to mosquito larval control with less ecological and health risks of drug resistance development. Plant and marine macroalgal-derived agents show promise as effective but eco-friendly and drug-resistant risk-free approaches to mosquito larval control[10].Marine macroalgae, also referred to as marine plants or seaweeds, provide an enormous, renewable resource of variously structured bioactive compounds that have a number of ecological as well as biomedical applications. Marine macroalgae belong to several major phyla, namely, brown marine algae (Phaeophyceae), red marine algae (Rhodophyta), and green marine algae (Chlorophyta). [11].The naturally occurring metabolites in seaweeds tend to be of lower toxicity but high biodegradability; thus, they are desirable candidates in vector control and other areas.

Recent research has emphasized some of the remarkable biochemistry associated with macroalgae and its ability to deliver safe and eco-friendly agents with possible uses as larvicides, repellents, free-radical scavengers, and antimicrobial compounds without adverse environmental impacts [12].Apart from their use in health and pharmacy-related activities, the metabolites present in macroalgae find applications in eco-friendly pest management activities and larvicidal compound development studies, during which the complex chemical composition of these compounds can interfere broadly within the physiological activities of insects without affecting the rest of the species or the environment [13]. These activities can be conducted sustainably by using the approach offered by the principles of the 'blue bio-economy,' which emphasizes the harvesting of these compounds in an environmentally friendly manner.Overall, these discoveries have placed marine macroalgae as an untapped source of eco-friendly bioactive compounds that hold promise in revolutionizing mosquito larval control and other fields where safe and sustainable biological resources are desired.

Marine macroalgae, or simply seaweeds, are multicellular photosynthesizing organisms that occur in marine and coastal ecosystems across the globe. They play a significant role in marine biodiversity and primary production. Moreover, they function as ecological keystone species. Compared to plants that have roots, stems, and leaves, macroalgae do not have these structures. However, they develop adapted structures that have emerged specifically to carry out functions such as nutrient uptake and photosynthesis[14]. Depending on various biochemical properties and colors, marine macroalgae have grouped these primary photosynthesizers into three large sections. They include brown algae belonging to class Phaeophyceae, green algae classified under class Chlorophyta, and red algae classified within class Rhodophyta. Combining these sections, an impressive variety of primary and secondary metabolites is formed, facilitating adaptation to various abiotic and biotic pressure components such as grazing, sunlight, and vector pressure that various populations of macroalgae experience [15]. In various ways, these macroalgae metabolites have applications. Generally, they are used as pharmaceutical, cosmetics, vector control, and agriculture research tools.

Classification of Marine Macroalgae

Green Algae (Chlorophyta)

Green macroalgae contain chlorophyll a and b, which give them their characteristic green coloration, as in the case of terrestrial plants. They are generally found in shallow marine waters with rich illumination and can dominate shallow intertidal zones. Chlorophyta are rich in bioactive metabolites such as amino acids, fatty acids, polysaccharides, polyphenols, and pigments responsible for antioxidant, immunoregulatory, and

anti-inflammatory functions. It is established that Chlorophyta, while relatively less rich in secondary metabolites than brown or red algae, contain alkaloids, terpenes, steroids, and glycerides with various bioactivities relevant to health and/or ecological interactions [16].

Brown Algae (Phaeophyceae)

The chloroplasts in Brown algae have chlorophyll a and c, along with lycopene, allowing them to have a brownish appearance that helps them in utilizing the sunlight in deep or temperate waters. The members of this class have large kelps with many common members like Sargassum, Fucus, and Laminaria. The Brown algae have been cited in literature to be rich in sulfated polysaccharides like fucoidans, phlorotannins (polyphenolic compounds), and sterolics, many of them having strong antioxidant activity along with antiviral, anticoagulant, and antimicrobial potential [17].

Red Algae (Rhodophyceae)

The bioactive compounds frequently found in red macroalgae are chlorophyll a, phycoerythrin, and phycocyanin. These have distinct blue and green absorbances and are responsible for their growth at greater depths. Rhodophyta appear to represent the macroalgae with the greatest number of species and are important producers of sulfatedgalactans as well as fatty acids and other phenolic substances. The phenolic substances have antioxidant, antimicrobial, anti-inflammatory activities and also anti-tumoractivities[18].The marine macroalgae produce a wide array of secondary metabolites, compounds not involved directly with growth or reproduction, for ecological defense.

The functions and possessing useful biological activities:

Sulfated polysaccharides include the likes of fucoidans, carrageenans, and ulvans, which confer antioxidant, antiviral, immunomodulatory properties, and anticoagulant properties.Polyphenols and Phlorotannins: They are abundant, especially in brown algae, and show a high antioxidant and UV-protective activities.Pigments-carotenoids, chlorophylls, and phycobilins: fucoxanthin and phycoerythrin, for example, play antioxidant and photoprotective roles.These are terpenoids and sterols[19],which represent a diversity of structures with reportedly anti-inflammatory, antimicrobial, and cytotoxic activities.Fatty Acids: besides providing important essential polyunsaturated fatty acids.Proteins and Peptides: these have also been reported to possess antioxidant and immunoregulatory functions.

Such diversity is also seen in their adaptation to survive different marine ecological niches. The significance of these compounds also lies in their investigation towards nutraceutical and pharmaceutical industries and also as eco-friendly pest control agents, like mosquito larvicidal compounds that have the potential to restrict mosquito breeding with minimal impact on the environment[20]Mosquitoes (family Culicidae) are medically significant vectors responsible for the transmission of a range of pathogens that cause malaria, dengue, chikungunya, Zika, West Nile fever and lymphatic filariasis.

Mosquito Larvae and Larvicidal Activities

Understanding species biology is key when evaluating larvicidal strategies and some common vectors are, Aedes aegypti — A primary urban vector of dengue, Zika, chikungunya and yellow fever. It typically breeds in artificial containers and small water bodies. Its larval ecology favors urban habitats with temporary, small water reservoirs [21]. Anopheles stephensi — A major malaria vector in South and Southeast Asia. Larvae thrive in a range of water bodies which including domestic wells and ponds, and show ecophysiological adaptability [22]. Culex quinquefasciatus — A vector of lymphatic filariasis and West Nile virus in tropical and subtropical regions. It exploits polluted or stagnant waters for breeding [23].Marine macroalgae and their secondary metabolites have been assessed for larvicidal activity against these three key vector species, with several studies showing significant mortality at low concentrations (e.g., LC_{50} values in the microgram range for seaweed extracts) [24].

Mosquito larvae undergo four distinct instar stages before pupation, all of which are aquatic and represent optimal targets for larvicidal control measures because larvae are relatively immobile and concentrated in discrete habitats. Egg → Larva → Pupa → Adult: After eggs hatch in water, larvae feed on organic matter, microorganisms, and algae. Larvae molt through first to fourth instars over days depending on temperature, food and species[25].Larval Physiology: Larvae possess specialized structures such as breathing siphons (Aedes and Culex) and mouth brushes for feeding. Their digestive tract, midgut epithelial cells, cuticle lining and nervous system are central to metabolic processes and represent points of physiological vulnerability[26].

The Larval stages occupy water surfaces or water columns where they filter feed — an ecological niche that makes them accessible to water-soluble larvicides and bioactive compounds that can disrupt feeding, respiration and growth[27]. Larval stages are particularly sensitive to toxic compounds because their cuticle and immature detoxification systems are not fully developed. Disruption of key physiological pathways such as enzyme activity, midgut integrity, or ion transport readily leads to mortality at low concentrations.Natural larvicides — including extracts from marine macroalgae, exert toxicity through multiple, often synergistic mechanisms, many of which have been identified in recent research:

Disruption of Cellular and Midgut Integrity

Several seaweed extracts cause direct damage to larval midgut epithelial cells, which are critical for nutrient absorption and barrier function: Phenolic compounds and fatty acids present in macroalgae can compromise

larval cell membranes, leading to cell lysis and tissue breakdown[28].Histopathological effects such as midgut epithelial damage and disordered tissue organization have been observed in larvae treated with bioactive extracts from marine algae and related plant sources [29].

Oxidative Stress and Enzyme Inhibition

Bioactive compounds generally act by inducing oxidative stress in larvae due to an increase in reactive oxygen species and overwhelming antioxidant defenses, It has been reported that algal extracts and algae-based nanoparticles induce oxidative damage, disrupt mitochondrial function, and interfere with energy metabolism in larvae[30]. It reduces the larva's ability to process nutrients and clear toxic metabolites by inhibiting key enzymes in digestion and detoxification pathways, including proteases, esterases, and detoxifying oxidases. These physiological processes being disrupted lead to weakened larvae that result in growth inhibition or death[31].

Interference with Growth and Development

Certain macroalgae compounds impact hormonal and metabolic pathways essential for larval development, By altering larval hormonal regulation or disrupting enzyme activities associated with molting and metamorphosis, extracts can prolong larval duration or prevent pupation.

Neurotoxicity and Behavioural Effects

Some larvicidal compounds may interfere with the larval nervous system, Although less studied for macroalgal extracts specifically, many botanical larvicides act on neural targets (such as acetylcholinesterase inhibition) which impair mobility and survival[32].

Larvicidal Activities of Macroalgae

Macroalgae contain mixtures of phenolics, terpenoids, alkaloids, fatty acids and other metabolites. These can work together to produce synergistic toxicity, disrupt multiple physiological systems at once, and reduce the likelihood of resistance developing[18].

Targeting larval stages of Aedes, Anopheles and Culex species represents an effective strategy for vector control because larvae are aquatic, localized, and physiologically vulnerable. Marine macroalgae and algae-derived bioactive present a rich source of eco-friendly larvicidal agents that impact multiple biological pathways — from gut integrity and metabolic enzyme function to oxidative stress and development inhibition. Understanding these targets and mechanisms — particularly in the context of environmentally sustainable mosquito management — is essential for advancing larvicide research beyond conventional insecticides[33]Figure 1.

Extraction of bioactive compounds from marine macroalgae (seaweeds) is a critical step in evaluating their larvicidal activity against mosquito larvae. The choice of solvent and method influences both the quantity and nature of secondary metabolites extracted (e.g., phenolics, terpenoids, flavonoids) and consequently affects larvicidal potency[29]. Common Solvents Used in Macroalgae Extraction are Aqueous Extracts – Water extracts polar components such as polysaccharides and some glycosides. These can have limited mosquito larvicidal activity unless concentrated or enhanced. Methanolic Extracts – Methanol is a polar organic solvent effective for extracting phenolics[15],flavonoids and other polar metabolites with bioactivity. Ethanolic Extracts – Ethanol extracts similar polar to mildly polar compounds. Many studies report significant larvicidal activity with ethanolic extracts [34].Hexane and Other Non-Polar Extracts – Hexane primarily extracts non-polar compounds such as fatty acids, terpenoids, and some lipophilic allelochemicals that are often potent against mosquito larvae. Chloroform / Dichloromethane / Acetone / Ethyl Acetate – Medium-polarity solvents that can extract a range of bioactive molecules and often exhibit high larvicidal effects in empirical assays[35].Intertidal activity of Marine Algae such as Green Algae, Brown Algae and Red Algae as shown in following (Table1) (Table 2) and (Table 3).

Table 1. The ability of green algae (Chlorophyta) to eradicate mosquito larvae.

GreenAlgaeSpecies	Target Pest (Mosquito Species)	Products/Effects (Active Compound or Extract Type)	Reference Paper
Ulva lactuca	Aedes aegypti (Larvae)	Methanol extract; LC_{50} = 42.7 µg/mL	[36]
Ulva fasciata	Anophelesstephensi(Larvae)	Ethyl acetatefraction; LC_{50} =58.3 µg/mL	[37]
Caulerparacemosa	Culexquinquefasciatus (Larvae)	Caulerpin(alkaloid); LC_{50}= 1.8 mg/mL	[38]
Caulerpascalpelliformis	Aedes aegypti (Larvae)	Acetone extract; LC_{50} = 72.4 µg/mL	[38]
Enteromorphaintestinalis	Anophelesgambiae (Larvae)	Chloroform extract; 100%mortality at 250 ppm	[39]
Codium fragile	Culex pipiens (Larvae) (Figure 1)	Sulfatedpolysaccharides;LC_{50} = 0.85 mg/mL	[40]

Chaetomorphaantennina	Aedes albopictus (Larvae)	Methanol extract; LC_{50} =95.2 µg/mL	[39]
Halimeda opuntia	Anophelesstephensi (Larvae)	Diterpenes(Halimedatrial); LC_{50} =12.5 µg/mL	[39]
Cladophora glomerata	Culextritaeniorhynchus (Larvae)	Hexane extract; LC_{50} =110.5 µg/mL	[40]

(Table 1; LC_{50}- Lethal concentration 50 %, µg- mew gram, mL- milli litre, ppm- parts per million)

Table 2. The ability of brown algae (Phaeophyceae) to execute mosquito larvae.

Brown Algae Species	**TargetPest(Mosquito Species)**	**Products/Effects (Active Compound or Extract Type)**	**Reference Paper**
Sargassum wightii	Aedes aegypti (Larvae)	Methanol extract; LC_{50} = 48.2 µg/mL	[41]
Turbinaria ornata	Anopheles stephensi (Larvae)	Chloroform-methanol (2:1) extract; LC_{50} = 35.7 µg/mL	[38]
Padina gymnospora	Culex quinquefasciatus (Larvae)	Hexane fraction containing sterols; LC_{50} = 42.5 µg/mL	[42]
Dictyota dichotoma	Aedes albopictus (Larvae)	Diterpenes (Dolastanes); LC_{50} = 12.8 µg/mL	[41]
Sargassum ilicifolium	Anopheles culicifacies (Larvae)	Polyphenol-rich ethyl acetate extract; 100% mortality at 250 ppm	[38]
Ecklonia maxima	Culex pipiens (Larvae)	Phlorotannin-enriched extract; LC_{50} = 0.92 mg/mL	[42]
Fucus vesiculosus	Aedes aegypti (Larvae)	Fucoidan (sulfated polysaccharide); LC_{50} = 1.2 mg/mL	[41]

(Table 2; LC_{50}- Lethal concentration 50 %, µg- mew gram, mL- milli litre)

Table 3. The ability of Red Algae (Rhodophyta) to execute mosquito larvae.

Red Algae Species	**Target Pest (Mosquito Species)**	**Products/Effects (Active Compound or Extract Type)**	**Reference Paper**
Gracilariacorticata	Aedes aegypti (Larvae)	Methanol extract; LC_{50} = 52.4 µg/mL	[43]
Kappaphycusalvarezii	Anopheles stephensi (Larvae)	κ-carrageenan (sulfated polysaccharide); LC_{50} = 1.05 mg/mL	[38]
Laurencia obtusa	Culex quinquefasciatus (Larvae)	Brominated sesquiterpenes; LC_{50} = 9.8 µg/mL	[44]
Asparagopsistaxiformis	Aedes albopictus (Larvae)	Bromoform (halogenated compound); LC_{50} = 6.5 µg/mL	[38]
Hypneamusciformis	Anopheles gambiae (Larvae)	Ethanol extract; LC_{50} = 67.3 µg/mL	[44]
Plocamiumcartilagineum	Culex pipiens (Larvae)	Polyhalogenated monoterpenes; LC_{50} = 11.2 µg/mL	[45]
Gelidiumserrulatum	Aedes aegypti (Larvae)	Aqueous extract (phycocolloids); LC_{50} = 1.8 mg/mL	[45]

(Table 3; LC_{50}- Lethal concentration 50 %, µg- mew gram, mL- milli litre)

Table. 4. Mode of Action of Marine Macroalgae in Mosquito Larvae: -

Mode of Action	Primary Target / Pathway	Observed Effects in Larvae	Marine Macroalgae & Bioactive Compounds	Target Mosquito Species	Reference Paper
Enzyme Inhibition (Neuroenzymatic)	Acetylcholinesterase (AChE) inhibition	Accumulation of acetylcholine at synapses, paralysis, impaired nerve impulse transmission, larval mortality	Sargassum vulgare, Caulerpa racemosa, Padina tetrastromatica; phenolics, terpenoids, phlorotannins	Aedes aegypti, Aedes albopictus, Culex pipiens	[46]
Enzyme Modulation (Metabolic & Detoxification)	Digestive enzymes (amylase, protease); detox enzymes (esterases, GST, CYP450)	Disruption of digestion, metabolic imbalance, inability to detoxify toxic compounds	Ulva lactuca, Sargassum wightii, Gracilaria edulis; fatty acids, flavonoids	Aedes aegypti, Culex quinquefasciatus	[31]
Gut Epithelium Disruption	Midgut epithelial cells	Vacuolization, epithelial degeneration, damaged microvilli, leakage of gut contents leading to starvation and death	Bryopsis pennata, Padina gymnospora, Dictyota dichotoma; cytotoxic secondary metabolites	Aedes aegypti, Aedes albopictus, Culex tritaeniorhynchus	[47]
Histopathological Alterations	Midgut, anal papillae, cuticle	Tissue necrosis, cell lysis, distorted body segments, impaired osmoregulation	Brown and red seaweeds (Sargassum, Gracilaria)	Aedes aegypti	[48]
Neurotoxic Effects	Nervous system signaling pathways	Tremors, abnormal movement, loss of coordination, paralysis	Terpenoids, alkaloids, phenolics from brown macroalgae	Aedes aegypti, Culex pipiens	[49]
Growth Regulatory Effects	Endocrine signaling (ecdysone, juvenile hormone balance)	Prolonged larval duration, inhibited pupation, malformed pupae, reduced adult emergence	Sargassum spp., Caulerpa spp.; sterols, growth-regulating metabolites	Aedes aegypti, Aedes albopictus	[50]
Morphological Deformities	Cuticle and external structures	Deformed head capsule, damaged siphon, anal papillae	Padina, Ulva, Gracilaria extracts	Aedes aegypti,Anophelesstephensi	[51]

		destruction			
Respiratory Impairment	Tracheal and siphonal systems	Reduced oxygen uptake, suffocation, lethargy	Lipophilic compounds from brown seaweeds	Aedes aegypti, Culex spp.	[52]
Synergistic Nanotoxic Effects	Enhanced penetration of bioactives	Increased larvicidal potency due to improved delivery and enzyme interaction	Ulva lactuca, Sargassum wightii-mediated Ag/ZnO nanoparticles	Anopheles gambiae	[53]
Multiple-Target Toxicity (Cumulative Effect)	Nervous, digestive, endocrine systems	Rapid mortality due to combined enzyme inhibition, tissue damage, and developmental arrest	Mixed macroalgal extracts (brown, red, green algae)	Multiple mosquito vectors	[54]

(GST- Glutathione S-transferase, CYP450: Cytochrome P450, Ag: Silver,ZnO: Zinc Oxide)

Conclusion and Future Prospects

Diseases that mosquitoes spread are still a major global public health and economic problem. This means that we need to come up with safer, more sustainable, and more resistant vector control solutions. The evidence compiled in this review indicates that marine macroalgae—encompassing green, brown, and red algal groups—constitute a substantial and predominantly underutilized reservoir of potent larvicidal compounds, including sulfated polysaccharides, phenolics, terpenoids, sterols, and fatty acids, many of which demonstrate significant efficacy at low concentrations against principal mosquito vectors such as Aedes, Anopheles, and Culex. Macroalgal-derived bioactives, in contrast to traditional synthetic larvicides, operate via various physiological mechanisms, such as enzyme inhibition, disruption of gut epithelium, induction of oxidative stress, and regulation of growth. This multifaceted action diminishes the probability of resistance emergence while reducing ecological and non-target toxicity. Future research should concentrate on the standardization of extraction procedures, the identification and characterization of active principles, the assessment of field-level efficacy, and the incorporation of macroalgal larvicides into environmentally sustainable vector control frameworks that adhere to the principles of the blue bioeconomy.

Authors' contributions

VS, IS, KP, GJ &TA conceived the research, assisted in its design, execution, and analysis, as well as data interpretation and manuscript writing. **AT** helped with the implementation of the experiment as well as the manuscript revision. The manuscript was written by both contributors, who also provided feedback. The final manuscript has been read by all writers and authorized.

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Data availability

Data will be made available on request.

Consent to publish

Not applicable.

Competing interests

The authors declare no competing interests.

Ethical approval and consent to participate

Not applicable.

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