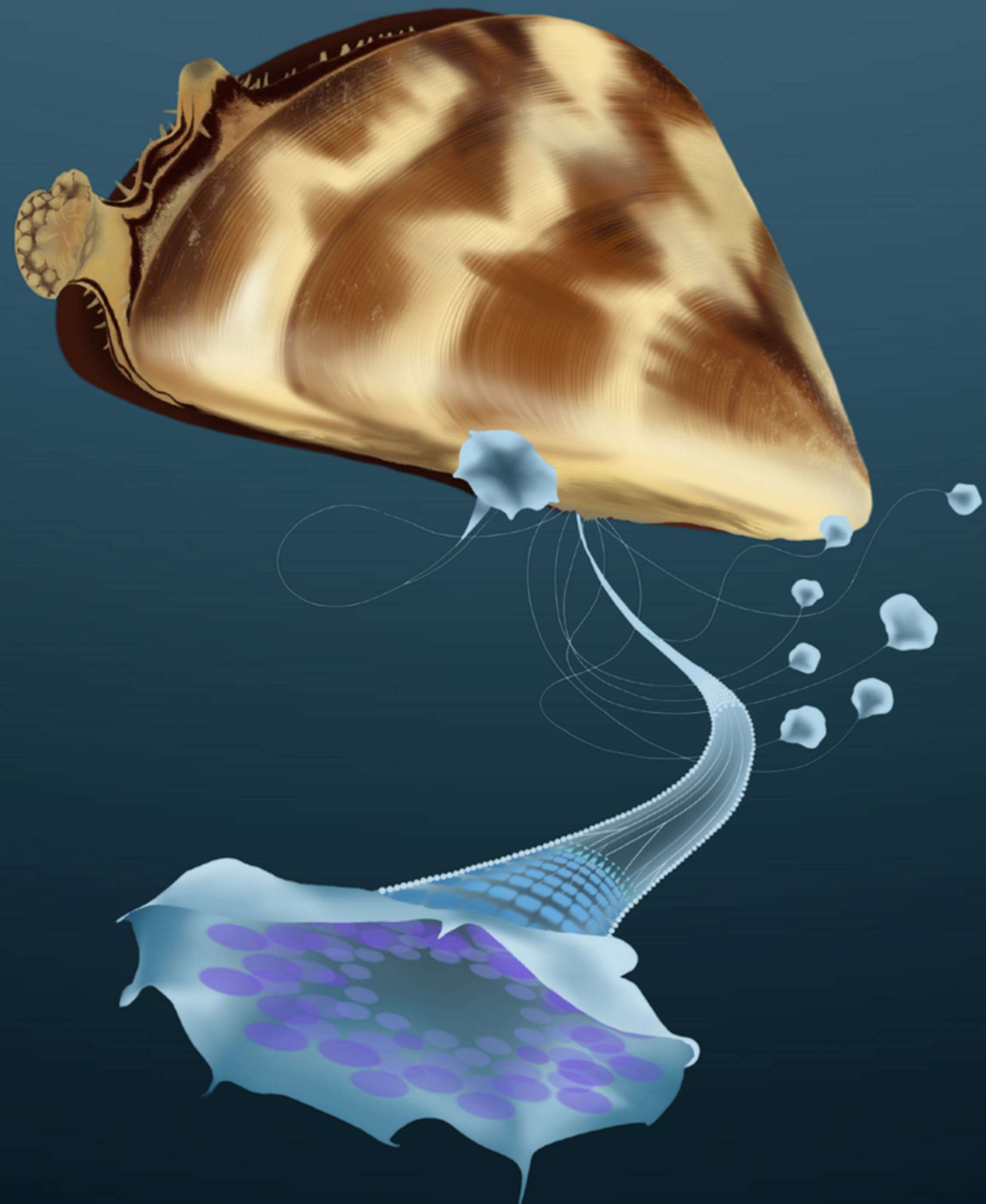

Zebra Mussel Adhesive Glue as an Alternative to Current BPA-based Composites in Dental-Orthodontic Treatment.

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INTRODUCTION

Bisphenol A (BPA) is an organic compound most commonly used in the manufacturing of plastics, epoxy resins, and other polymers.[1] Through exposure to high temperatures and use, BPA's epoxy coating can wear off, leading it to contaminate its surroundings. From there, BPA can make its way into the human system through the oral cavity and into the digestive tract.[2] BPA exposure in humans originates from the oral cavity and can make its way through the digestive tract. Upon initial exposure in the human body, it is readily metabolized by the liver and excreted through the urine within 24 hours.[3] Frequent absorption of BPA can affect different bodily systems.[4] Common dental treatments for tooth protection, restoration and alignment use composite filling material, sealants, and orthodontic adhesives. According to the American Dental Association (ADA), once these adhesive substances are applied on the teeth, BPA is released in the saliva within 24-48 hours.[5]

Although the exposure is low and past literature is uncertain of the adverse effects of it, recent studies show that BPA exposure may elicit non-monotonic effects, suggesting that low doses are more vital than the latter, causing endocrine abnormalities.[6] This uncertainty led to the European Food Safety Authority (EFSA) reducing the Tolerable Daily Intake (TDI) of BPA from 50 ug/kg bw/day in 2006 to 5 ug/kg bw/day in 2012.[7] As the demand and access to dental treatment, especially for low SES (socioeconomic status) Canadians, continues to rise, low-dose BPA exposure in humans will continue to increase.[8] Therefore, a sustainable approach to administering treatment to reduce unnecessary exposure to BPA is required. We propose to combat this issue by integrating an environmentally friendly, fluid resistant, permanent molecular bioadhesive naturally found in zebra mussels.

KNOWN HEALTH EFFECTS

Although BPA levels are typically under the daily intake threshold (4 ug/kg bw/day) and are efficiently excreted, there is evidence of "low dose effects" and the rise of medical disorders due to elevated BPA levels in urine.[4] Research suggests that BPA can disrupt the endocrine system by mimicking the hormone estrogen, leading to various health risks.[9] One major concern is its potential to interfere with reproductive health. BPA exposure has been linked to infertility, miscarriages, and hormonal imbalances.[10] Furthermore, studies conducted by the Department of Bioengineering at the University of Texas at Arlington have associated BPA exposure with

an increased risk of certain cancers, such as breast and prostate cancer. It also leads to cardiovascular diseases and metabolic disorders like obesity and diabetes.[11] Given these risks, there is a pressing need for alternatives to BPA in various industries, including dentistry. Dental materials, such as sealants and composites, have traditionally contained BPA, potentially exposing patients to its harmful effects during dental procedures. Developing BPA-free alternatives for these dental products is crucial to minimize exposure and safeguard the health of both patients and dental professionals.[4]

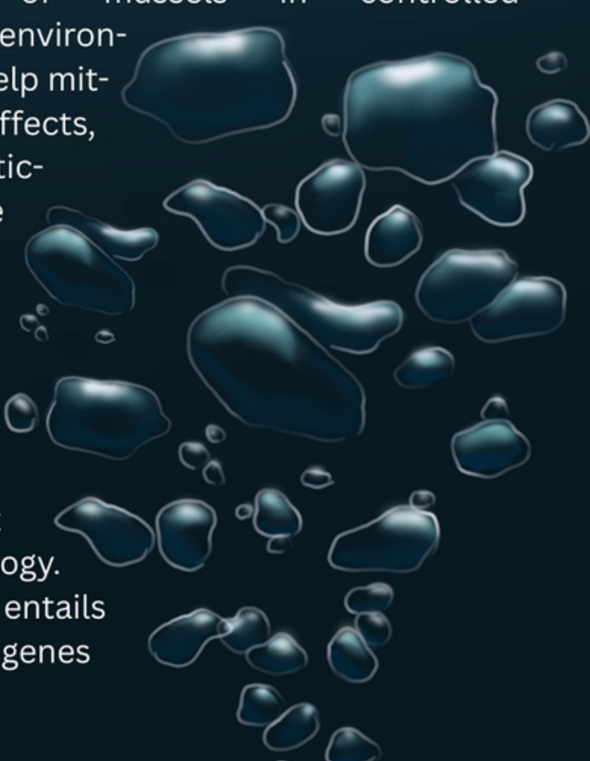
ZEBRA MUSSEL ADHESIVE

Zebra mussels secrete glue-like fibers called bissell threads to anchor themselves underwater whilst withstanding strong waves and currents. These threads exhibit the ideal properties required for in clinical bioadhesives such as curing in wet environments, hydrophilicity, hydrogen bonding, and crosslinking formation capability.[11]

The basis of the mussels' adhesive characteristic stems from the secretion of 6 mussel adhesive proteins (MAPs). These MAPs contain high levels of 3,4 dihydroxy phenylalanine (DOPA), which are the main factor in mussels' underwater adhesive capabilities. DOPA specifically contributes to the interfacial attachment and curing of adhesive plaque proteins. These molecules are chemically versatile as they can attach to both organic and inorganic surfaces via reversible non-covalent bonds, allowing mussels to establish connections to surfaces, and being able to detach if necessary.[11] DOPA can also form strong hydrogen bonds, through dihydroxyl functionality (intermolecular bonds between -OH groups), allowing it to readily bind to tissue surfaces such as mucosa. This bioadhesive is deemed to be compatible with the oral cavity, as mussel based mucoadhesives have been synthesized in the past as drug delivery carriers. This process releases localized antibiotics and growth factors to prevent infections and promote wound healing.[11] A specific example is an oral paste called 'Orabase', a mucoadhesive derived from mussels that delivers penicillin used to treat mouth ulcers. This adhesive is a highly accessible substance which can be extracted from these invasive species which have a high reproduction rate. This results in their excessive feeding on phytoplankton populations which are a primary source for 50% of the available oxygen needed to sustain life in the biosphere.[12, 13]

PRODUCTION & EXTRACTION

The extraction of MAP can be potentially harmful to the animals if not conducted sustainably. Traditional extraction methods involve harvesting and dissecting mussels to access their adhesive-producing glands, which is typically an invasive and lethal method.[14] Non-lethal harvesting techniques, and the cultivation of mussels in controlled aquaculture environments can help mitigate these effects, but the practicality of these methods is limited.[14] A more sustainable approach involves recombinant DNA technology. This method entails isolating the genes responsible for MAP production and inserting them into microorganisms, such as bacteria or yeast, to produce MAP in large quantities without harming mussels. The sustainable production of MAP is important to protect the biodiversity and habitat for marine life as zebra mussels, while invasive, serve as filter feeders - consuming excess nutrients and organic matter and thereby, improving water clarity and reducing the risk of harmful algal blooms. This biotechnology approach is scalable and can potentially yield several grams to kilograms of MAP per fermentation batch, providing a cost-effective and environmentally friendly solution .[14, 15] Unlike traditional extraction methods, recombinant production systems can continuously produce large quantities of MAP. Though the initial setup for recombinant methods can take several months, the production cycle itself typically takes only a few days to a week per batch.[11]



LONG-TERM IMPLICATIONS & NEXT STEPS

The long-term implications of using MAP in dental applications are promising. Medically, MAP is biocompatible, reducing the risk of adverse reactions and toxicity associated with BPA.[11, 14]

Unlike BPA, which has been linked to hormonal disruptions and associated health risks, MAP poses minimal health risks, enhancing patient safety and acceptance of dental treatments.It is important however, to consider the social implications of MAP usage. For one, individuals may be opposed to having foreign mussel-produced substances in their mouths. These sentiments may be amplified by barriers to science communication such as misinformation and disinformation. As a result, to supplement these changes, it is crucial that educational workshops (with a focus on health literacy) are conducted to guide and inform others on MAP usage, with an emphasis on its benefits and area of improvement. Economically, the initial costs of developing MAP-based adhesives are high due to the research and regulatory approval processes. However, once established, MAP production via recombinant DNA technology can be cost effective and scalable. Over time, this widespread adoption could potentially reduce costs related to BPA exposure, such as treatments for hormone-related conditions.[15] Furthermore, the environmental impact of using MAP is lower than synthetic chemicals.

Sustainable production methods, including non-lethal harvesting and recombinant DNA technology, can minimize ecological footprints and support conservation efforts.[16] However, with any novel development, there are limitations. There is limited information regarding the oral stability of MAP as an adhesive. For instance, the question of whether it would interact negatively with already existing oral secretions (such as saliva) remains unanswered. Further research is required to investigate the compatibility of surface adhesive proteins like MAP in the oral cavity. Ultimately, with ongoing research, transitioning to MAP-based dental adhesives will enhance patient safety, offer cost-effective solutions, and promote environmental sustainability, leading to broader long-term benefits for public health and the economy.

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