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LETTER TO EDITOR
MARINE RESOURCES: POTENTIAL OF POLYCHAETE APPLICATION IN COMBATING COVID-19 INFECTION

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Abstract: An antiviral vaccine for COVID-19 is not yet available. Research on polychaete has revealed the ability of its purified haemoglobin in assisting oxygenation to vital organs. Polychaete's blood and tissue extracts were used as an oxygen-carrier and as a reducing agent in the biosynthesis of silver nanoparticles (Ag-NPs), respectively. Polychaete-based oxygen carrier can be used in organ preservation and as potential treatment for near-death COVID-19 patients. Ag-NPs from polychaete, which are known for possessing excellent antimicrobial properties, may serve as a raw material for various products, including disinfectant, coating materials for paint, handrail, personal care and healthcare products, such as personal protective equipment (PPE). The COVID-19 pandemic may be a catalyst to unveil hidden potentials of polychaete, particularly its therapeutic properties in medicine.

Keywords: Antivirus, silver nanoparticles, haemoglobin, oxygen-carrier, polychaete

Abbreviations: *AgNPs, COVID-19, PPE.*

Introduction

Coronavirus Disease 2019 (COVID-19) is very infectious and was first reported in Wuhan, China (van Doremalen *et al.*, 2020). The respiratory illness was identified in December 2019, causing population lockdowns, economic upheaval and mass suffering as it spreads across the globe. To date, more than 31 million cases have been reported worldwide, with the death toll reaching almost one million (World Health Organization, 2020). COVID-19 is caused by the Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2), which belongs to the positive-sense single-stranded RNA virus of the *Coronaviridae* family in the genus *Betacoronavirus* (Guo *et al.*, 2020). Current research pertaining to this enveloped virus indicates that it is originated from bats due to genetic similarities to bat coronaviruses (Shereen *et al.*, 2020). Pangolins have been identified as potential hosts in facilitating human transmission (Zhang *et al.*, 2020).

SARS-CoV-2 transmission primarily occurs via respiratory droplets, which are produced by sneezing and coughing (Whannell, 2020). Another possible mode of transmission is direct contact with virus-contaminated surfaces (van Doremalen *et al.*, 2020). Once the virus enters the human body, it binds to the angiotensin-converting enzyme 2 (ACE2) on the membrane of alveolar epithelial cells, which serves as an entry point for the virus to hijack the host cells' metabolism to replicate, causing severe lung infection and breathing difficulty to the patient (Danser *et al.*, 2020; Letko *et al.*, 2020). Gastrointestinal organs are also profoundly affected because of considerable ACE2 expression in the tissues (Xu *et al.*, 2020). Similarly, high expression of ACE2 is observed in hypertensive or diabetic individuals as they are usually prescribed with ACE2-stimulating drugs (Fang *et al.*, 2020; Kulkarni *et al.*, 2020; South *et al.*, 2020).

Common symptoms of SARS-CoV-2 infections include fever, tiredness, shortness of breath and dry cough (Chen *et al.*, 2020). Most symptoms are mild, but serious complications may develop. In some cases, if pneumonia sets in, this may progress to diffuse alveolar damage (DAD), causing acute respiratory distress syndrome (ARDS) (Heymann & Shindo, 2020). Once COVID-19 becomes severe, the patient will require breathing aid, such as mechanical ventilation, due to organ failure. However, some infected individuals may remain asymptomatic and are able to spread the virus, making the disease difficult to curb (Bai *et al.*, 2020).

SARS-CoV-2 infection may be prevented by increasing personal hygiene, including frequent hand-washing with soap or hand sanitiser, covering the mouth while coughing and sneezing, practising physical distancing and self-quarantine (Salehi *et al.*, 2020). Currently, there is no vaccine or specific antiviral for the treatment of COVID-19. However, a study in France had described the use of polychaete (*Arenicola* sp.), specifically its blood, as an oxygen carrier in treating severe COVID-19 (Whannell, 2020). Therefore, this article discusses the hidden potential of polychaete as treatment for the disease in advanced stage.

Polychaete and Its Uses

Polychaetes, or commonly known as the marine worms, are organisms that belong to the class Polychaeta under the phylum Annelida (Idris *et al.*, 2019). These marine worms are characterised by its bristles and segmented body. Polychaete can be in various sizes, ranging from one millimetre to six-metres in length (Nazri *et al.*, 2019). Approximately 11,456 polychaete species from 85 families have been identified (Pamungkas *et al.*, 2019). In Malaysia, Idris & Arshad (2013) stated that there are 64 polychaete species from 31 families that may be found in the country. Rosli *et al.* (2016) also identified 368 polychaete species in the southern South China Sea. More recent scientific expedition in 2019 covering the Peninsular Malaysia has discovered more than 60 polychaete families, with ongoing species identification still underway (unpublished data). Hence, Malaysia has diverse polychaete species with various potential uses.

Previous research on polychaetes were mainly focused on taxonomy. However, recent understanding of the ecological function and potential services have increased more scientific interest in this organism. Polychaete is an excellent bioindicator for pollution (Dean, 2008; Gaete *et al.*, 2017), high-quality food for aquaculture brood stocks and favourite bait for recreational fishing (Watson *et al.*, 2017; Cole *et al.*, 2018). In industrial and medical applications, it serves as a model for the production of nanomaterial and neurological disorder research (Idris *et al.*, 2019; Nazri *et al.*, 2019; Pei *et al.*, 2020).

During the COVID-19 pandemic, two hospitals in France embarked on a clinical trial using sandworm (*Arenicola marina*) blood to treat COVID-19 patients suffering from respiratory complications (VOA News, 2020). The sandworm blood was tested because of its ability to increase the oxygen level in the tissues of a patient whose respiratory system has been compromised — the haemoglobin in the worms' blood binds to oxygen 40 times greater than human haemoglobin when saturated (Rousselot *et al.*, 2006; Tsai *et al.*, 2012).

Subsequently, a biotechnology company called Hemarina in France has utilised the *A. marina* blood to produce purified haemoglobin called M101. The M101 has been successfully used as an "oxygen carrier" for organ preservation before a transplant (Thuillier *et al.*, 2019; Zachar, 2020). Its advantages include no immunogenic or allergic reactions, does not require any cofactors to function, and it simply releases its bound oxygen in a concentration-dependent manner (Rousselot *et al.*, 2006; Le Gall *et al.*, 2014; Le Meur *et al.*, 2020). Previous studies showed that organ preservation liquid containing M101 may lower the risk of oxidative damage to the organ as it provides oxygen molecules prior to the transplant (Thuillier *et al.*, 2011; Mallet *et al.*, 2014). Based on this finding, a clinical trial that involved human subjects was conducted with M101 as the organ preservative solution (Thuillier *et al.*, 2019; Le Meur *et al.*, 2020). Around 60 patients who received kidney transplants showed a faster recovery rate due to improve organ oxygen level compared with patients receiving kidney preserved in conventional preservative liquid (Le Meur *et al.*, 2020). Hence, this may be one potential treatment for severe COVID-19 patients who need assisted oxygenation in their vital organs. Nonetheless, the use of M101 is still at the early stage, requiring more comprehensive data.

Potential Benefits of Polychaete Derived-Silver Nanoparticles

In recent years, silver nanoparticles (Ag-NPs) are gaining recognition of their enhanced antimicrobial properties in comparison to its silver ion counterpart (Agnihotri *et al.*, 2014; Nakamura *et al.*, 2019). Ag-NPs are particles of silver ranging from 1 to 100 nm in size (Bedlovičová & Salayová, 2018; Hussain *et al.*, 2018). These particles possess unique physical, chemical and biological properties due to the large surface area per volume (Liao *et al.*, 2019). The excellent antimicrobial properties come from dissociation of Ag-NPs when exposed to oxygen and protons on the surface, releasing silver ions into the solution (Nakamura *et al.*, 2019). Ag-NPs are reported to have antiviral properties by acting on the virus surface, thus inhibiting its binding to host cells (Galdiero *et al.*, 2011; Khandelwal *et al.*, 2014). Previous studies showed that Ag-NPs were effective against several types of viruses, such as human immunodeficiency virus, influenza A virus, respiratory syncytial virus and hepatitis B virus (Gaikwad *et al.*, 2013; Lara *et al.*, 2010; Lv *et al.*, 2014; Morris *et al.*, 2019).

At present, there are three ways of synthesising Ag-NPs — chemical, physical and biological methods (Iravani *et al.*, 2014; Lee & Jun, 2019). The biological method is mostly favoured as it is simple, biocompatible and safe (Zhang *et al.*, 2016). Extract from plants and microorganisms have been previously used as a reducing agent in synthesising Ag-NPs. Nonetheless, a study by Singh *et al.* (2014) successfully used polychaete extract as a reducing agent, which raised additional interest to this organism. Synthesis of Ag-NPs using polychaete extract indicates the presence of bioactive compounds in polychaete cells that facilitate the synthesis process. The biosynthesised Ag-NPs demonstrated antimicrobial properties when tested against several pathogenic bacteria and viruses (Shameli *et al.*, 2011; Gaikwad *et al.*, 2013; Mori *et al.*, 2013). Interestingly, the extract of one local polychaete species, *Marphysa moribidii,* is also found to be able to synthesise Ag-NPs (Rosman *et al.*, 2020) and gold nanoparticles (AuNPs) with significant antimicrobial activity (Pei *et al.*, 2020). This shows that Ag-NPs from polychaete extract, particularly *M. moribidii,* can be further developed into various products that aids in combating COVID-19.

Other potential applications of Ag-NPs include as a disinfecting agent due to its broad-spectrum antimicrobial properties (Gopinath *et al.*, 2017). In Milan, Italy, a disinfectant solution comprising Ag-NPs and titanium dioxide nanoparticles have been developed for disinfecting buildings (Statnano, 2020). The company that produced the disinfectant claimed that any surface disinfected using the solution will remain sanitised for up to two years. This could be due to the constant release of antimicrobial ions from the nanoparticles on the surface. Moreover, Ag-NPs may be added into paint, coating materials and even fabric, which are used on frequently touched surfaces like handrails, doorknobs, smartphones and clothes (Reed *et al.*, 2016). Additionally, Ag-NPs can be formulated into personal care products, such as shampoo, deodorant and hand soap, to eliminate the presence of SARS-CoV-2 (Iravani *et al.*, 2014; Natsuki *et al.*, 2015; Lotfinejad *et al.*, 2020).

In fighting the pandemic, healthcare personnel use personal protective equipment (PPE) to prevent infection while treating patients. However, microbes and viruses may remain viable on the PPE that they wear. Therefore, improper removal and disposal of PPE will increase the risk of COVID-19 among healthcare workers (Nakamura *et al.*, 2019). To prevent this, biosynthesised Ag-NPs can be incorporated as the basic material in the production of PPE to offer greater protection. A study by Ishihara *et al.* (2015) found that chitin nanofiber sheets incorporated with Ag-NPs showed strong antimicrobial properties. Another study revealed that Ag-NPs can be easily incorporated into paper, cotton and cloths with nanoscale fibre surface (Nguyen *et al.*, 2014). Hence, adding Ag-NPs in materials to produce face masks, protective clothing, gloves, coats, bedding and medical apparatus, such as stethoscopes, will provide additional protection from infection among healthcare workers.

A recent finding by Zachar (2020) demonstrated the effective minimal inhibitory concentration (MIC) and safe level of Ag-NPs in inhalation delivery for COVID-19 treatment. Although subsequent studies are required, the results clearly showed that Ag-NPs are a promising antimicrobial agent in healthcare apparatus and treatment.

Future Prospects

This article discussed the potential applications of polychaete extract in treating and combating COVID-19. The current findings suggest that polychaete-based medical applications seemed promising. However, more studies are required to validate its medical importance in treating viral infections. Similarly, more in-depth studies on Ag-NPs synthesised from polychaete are needed, especially their mechanism of action in inhibiting viral replication. Assessment of Ag-NPs toxicity in animal cells is also required to prove its safety on human applications. Nevertheless, due to high diversity of Polychaeta, many of its health applications and benefits for humanity have yet to be discovered. This organism should gain more attention, admiration and protection. For these marine biomasses to provide man with further novel innovations, substantial taxonomic work is needed to identify the local wild stock population. Furthermore, sustainable aquaculture programmes are also required to reduce potential damage to the environment and extinction of potential polychaete species due to bait digging. Sustainable programmes are also needed to ensure their existence so more studies may be conducted on its medical applications.

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