polysaccharides

Review

Polysaccharide Stalks in *Didymosphenia geminata* Diatom: Real World Applications and Strategies to Combat Its Spread

Esther Somanader [1,2], Roshini Sreenivas [1], Golnoosh Siavash [1], Nicole Rodriguez [1], Tingxiao Gao [1,2], Hermann Ehrlich [1,2,3,4] and M. Azizur Rahman [1,2,*]

1 Centre for Climate Change Research, University of Toronto Entrepreneurship (ONRamp), Toronto, ON M5G 1L5, Canada; esther@climatechangeresearch.ca (E.S.); rosh.2992@gmail.com (R.S.); golnooshs@hotmail.com (G.S.); nicolerodri9@gmail.com (N.R.); tx.gao@mail.utoronto.ca (T.G.); Hermann.Ehrlich@esm.tu-freiberg.de (H.E.)
2 A.R. Environmental Solutions, ICUBE-University of Toronto, Mississauga, ON L5L 1C6, Canada
3 Institute of Electronic and Sensor Materials, TU Bergakademie Freiberg, 09599 Freiberg, Germany
4 Center for Advanced Technology, Adam Mickiewicz University, 61614 Poznan, Poland
* Correspondence: mazizur.rahman@utoronto.ca or aziz@climatechangeresearch.ca; Tel.: +1-647-892-4221

Abstract: *Didymosphenia geminata* is a species of freshwater diatom that is known as invasive and is propagating quickly around the world. While invasive species are generally considered a nuisance, this paper attempts to find useful applications for *D. geminata* in the biomedical field and wastewater remediation. Here, we highlight the polysaccharide-based stalks of *D. geminata* that enable versatile potential applications and uses as a biopolymer, in drug delivery and wound healing, and as biocompatible scaffolding in cell adhesion and proliferation. Furthermore, this review focuses on how the polysaccharide nature of stalks and their metal-adsorption capacity allows them to have excellent wastewater remediation potential. This work also aims to assess the economic impact of *D. geminata*, as an invasive species, on its immediate environment. Potential government measures and legislation are recommended to prevent the spread of *D. geminata*, emphasizing the importance of education and collaboration between stakeholders.

Keywords: chitin; diatoms; didymo; invasive species; polysaccharide structure; drug delivery; wound dressing; wastewater treatment; government legislation; economic impact

check for updates

Citation: Somanader, E.; Sreenivas, R.; Siavash, G.; Rodriguez, N.; Gao, T.; Ehrlich, H.; Rahman, M.A. Polysaccharide Stalks in *Didymosphenia geminata* Diatom: Real World Applications and Strategies to Combat Its Spread. *Polysaccharides* **2022**, *3*, 83–94. https://doi.org/10.3390/polysaccharides3010004

Academic Editor: Cédric Delattre

Received: 29 November 2021
Accepted: 3 January 2022
Published: 6 January 2022

1. Introduction

Diatoms are a type of unicellular microalgae that play a large role in the biosilica production and carbon fixation of the planet [1,2]. Additionally, they are also one of the largest producers of macronutrients such as nitrogen and phosphorus [1]. One species of freshwater diatom, *Didymosphenia geminata* (Lyngb.) has characteristic biomineralized polysaccharide stalks and blooms whose growth has recently proliferated throughout many aquatic ecosystems [3–6]. Although the invasive status of *D. geminata* may sometimes be uncertain, it is not the organisms themselves that have had the largest impact on the local environment but rather the adhesive stalks formed by *D. geminata* [7,8]. Unfortunately, the detailed chemistry of these fibrous structures has not been known until now. According to the modern view, these stalks are primarily composed of sulfated polysaccharides, proteins, and some uronic acid [3,4] and can spread and grow over 500 µm long and over multiple centimeters thick [8]. They are also able to divide during the cell reproduction process, leading to the production of large, branching, dense mats that can cover stream bottoms, covering areas of over 20 km [4,6,8]. Furthermore, the chemistry of the frustules of *D. geminata* has also not been well studied. Thus, the possible presence of a chitinous template within them, similar to that reported for the siliceous cell walls of marine diatoms [6,9–11], is still not confirmed. Research into this intriguing question is extremely important because chitin was not found in the stalks of this microalga and from this point of view, it would be illogical to find chitin inside the walls. Our recent investigation into the polysaccharide stalks of *D. geminata* (see Figure 1) shows how this diatom can build stalk-based layers on the rock surface and how the siliceous cells remain attached to biomineralized polysaccharide-containing adhesive stalks. The giant siliceous frustules of *D. geminata* may also have interesting biomedical and technological applications due to their highly specific micro- and nanoporous architecture (Figure 1B,C).

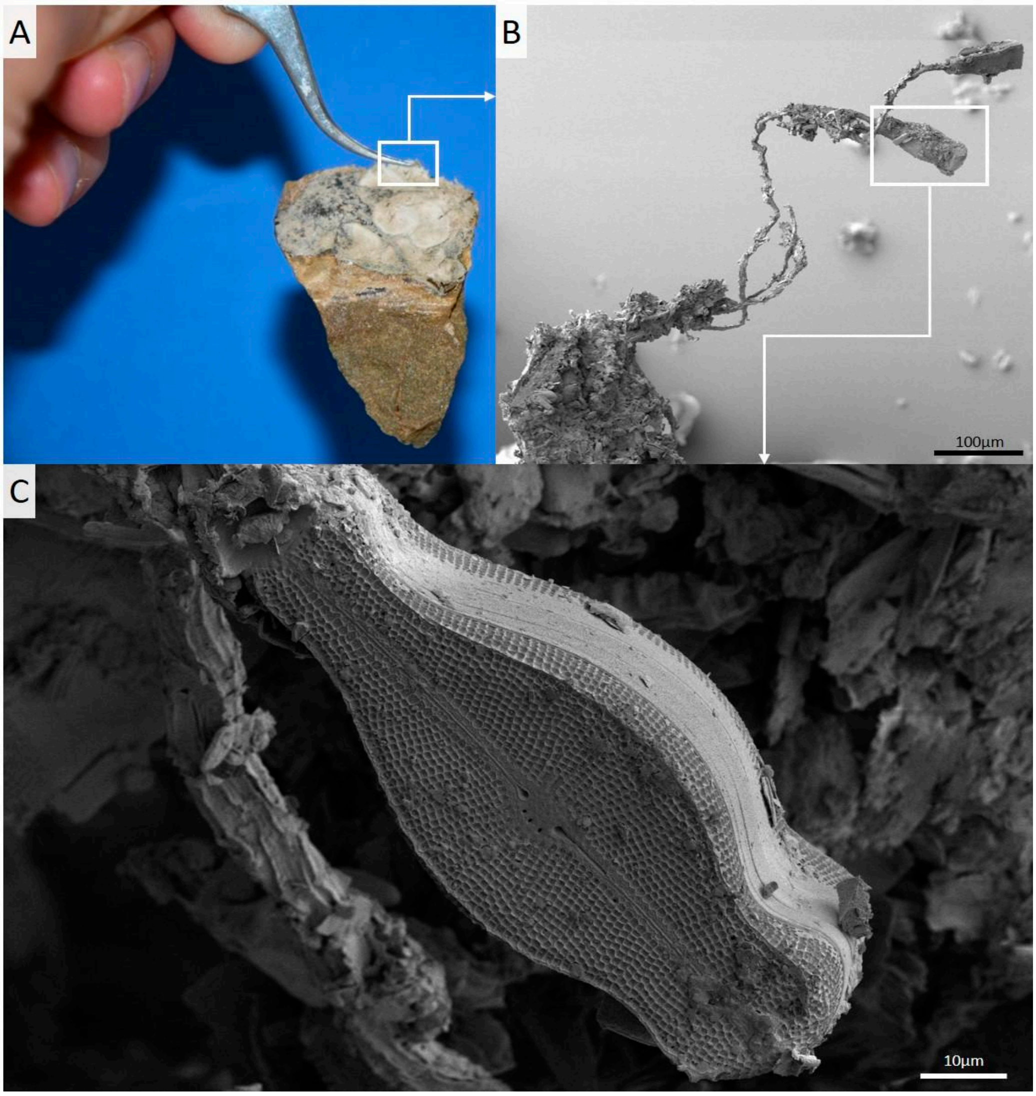

Figure 1. The diatom *D. geminata* can build stalk-based layers, which are responsible for very strong attachment to the rock surface (**A**). This felt-like layer has so firmly adhered to the surface of a hard substrate that a piece of stone can be held in the air, in a suspended state, without detaching from the ends of the tweezers. SEM images (**B**,**C**) show that siliceous cells remain attached to biomineralized polysaccharide-containing adhesive stalks.

D. geminata in benthic ecosystems has recently been a focus of research, in part due to the ability of blooms to manipulate and overwhelm the biodiversity of an ecosystem [12]. The presence of these large blooms alters local food-web structures by favoring smaller predators that can move between filaments and alter the composition of other diatoms [5]. The fish community is also affected by *D. geminata* blooms through changes to benthic invertebrate composition, with some New Zealand ecosystems experiencing a fish biomass decrease as a result [13]. The proliferation of *D. geminata* blooms also affects water quality, as diatom biodiversity and species composition are often used as measures of changes in environmental conditions [8]. Indeed, these blooms are caused by novel environmental conditions that are becoming increasingly more common due to climate change [14]. One of the largest predictors for the presence of polysaccharide blooms is the low concentration of dissolved phosphorus [7,15]. The formation of stalks is thought to be a way for *D. geminata* to elevate itself to reach the water column, where there is increased nutrient uptake [7,15,16]. While *D. geminata* bloom proliferation may have devastating effects on ecosystems, it can be suggested that its relatively large nanocalcite- and polysaccharide-based stalks may be used in many, more positive applications.

Here, we present a review of the recent literature focusing on the potential applications of *D. geminata*, including their use in wastewater treatment and as a biomaterial, based on the biological and chemical composition of its polysaccharide stalks. The motivation behind this emerging area of research is the unique structure of the microtubular stalks, which make them ideal reservoirs for small molecules, leading to their potential use in the aforementioned applications. Recently, *D. geminata* stalks have been shown to be effective in removing metallic ions such as Pb(II), Ni(II), and Cd(II) [4,17]. Because the stalks and frustules that are made of biogenic silica contain nontoxic, plant-based materials, they may also be ideal for biomedical applications or drug delivery [2,6,18,19]. Additionally, the environmental and economic impacts and environmental regulations of *D. geminata* are explored, and future policy recommendations are made. The research and recommendations we present in this review can be utilized for future studies regarding *D.geminata's* stalks. However, more research and progress is required with regard to the potential beneficial applications of *D. geminata* and the strategies to control its increasingly more common blooms.

2. Applications of *D. geminata* as a Biomaterial: Cell Adhesion, Proliferation, and Drug Delivery

D. geminata is a relatively new finding and has many potential uses in biomedicine and as a biomaterial for drug delivery, cell adhesion, and proliferation [6]. Principally, a biomaterial is defined as an inert material used in therapeutic or diagnostic procedures by interactions with components of living systems [20]. Polysaccharides are a great source of biomaterials, as they are naturally sourced, sustainable, and economically viable options due to their abundance in nature, including diverse aquatic niches. Chemically, polysaccharides are carbohydrates with repeating structures of monohydrides and are hence nontoxic by their very nature [18]. The polysaccharides in the stalk of *D. geminata* appear to be primarily sulfated xylogalactan, and the stalk was found to be intrinsically hydrophilic, a trait that is one of the first determiners of the extent of protein adsorption [21]. The presence of sulfate groups within polysaccharides shows an improvement in the immune system and would be beneficial to the nutraceutical industry [19]. The intrinsic biocompatible nature of *D. geminata* is attributed to its similarity in structure to glycosaminoglycans, which are a vital component in the tissue extracellular matrix [18].

Zglobicka in 2013 examined how previous studies had cast stalks of *D. geminata* as capable of adhering to multiple kinds of substrates because they were built in concentric circles of materials of variable compositions [22]. The chemical composition of the stalk seems to largely be unknown, but it is agreed that the main composition is amorphous silica [22,23]. The use of silica and biosilica in bone regeneration is well studied. It is understood to improve bone regeneration and increase bone density and is thought to play a role in the stabilization of collagen in the bone matrix [24]. The specific structure of *D. geminata* and its diatom frustules made of silica are especially beneficial with regard to drug delivery due to characteristics such as high permeability and low density [25].

D. geminata also exhibits anticancer properties [2]. As seen in Figure 2, the diatom has a nanosized porous silica capsule, which allows controlled drug release. The drug itself can be added to the external and internal surface of the diatom and then released based on need. The drug can be loaded onto the nanoparticles directly through noncovalent interactions like electrostatic bonding, hydrogen bonding, van der Waals forces, pi–pi stacking, and hydrophobic interactions [26].

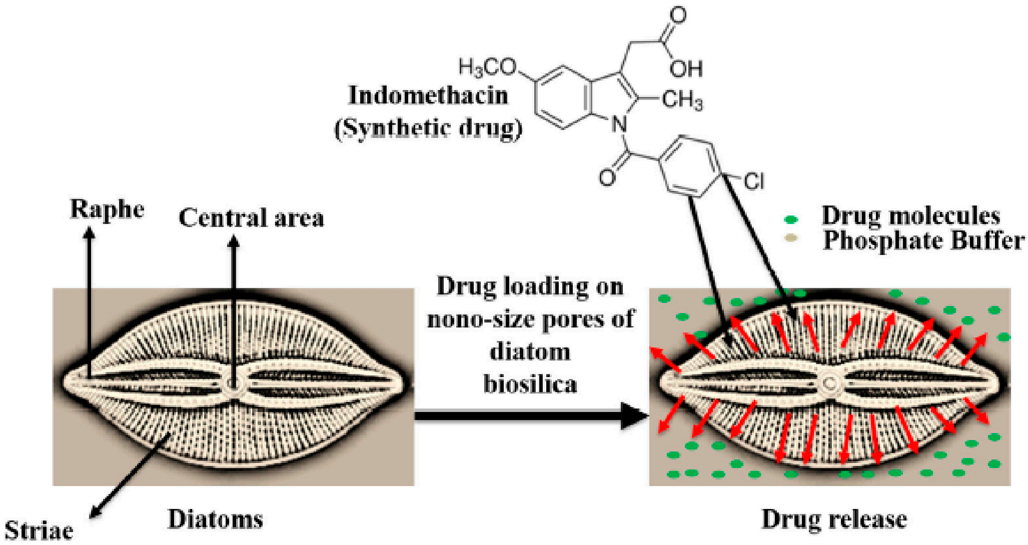

Figure 2. The mechanism of drug release from the porous diatom microshell [2].

The previous study also examined in some detail how the stalks formed by *D. geminata* can outlive the alga itself and are essentially a great substrate for cell adhesion [22]. Figure 3 shows a tubular structure of stalks. Further experimentation could involve examination of the interactions between a Didymo stalk as a substratum and a eukaryotic cell line in vitro. When testing a potential biomaterial for cell adhesion or cell proliferation in vitro, cellular models can be used to test the initial host response in addition to cell adhesion, proliferation, and cytotoxicity [27].

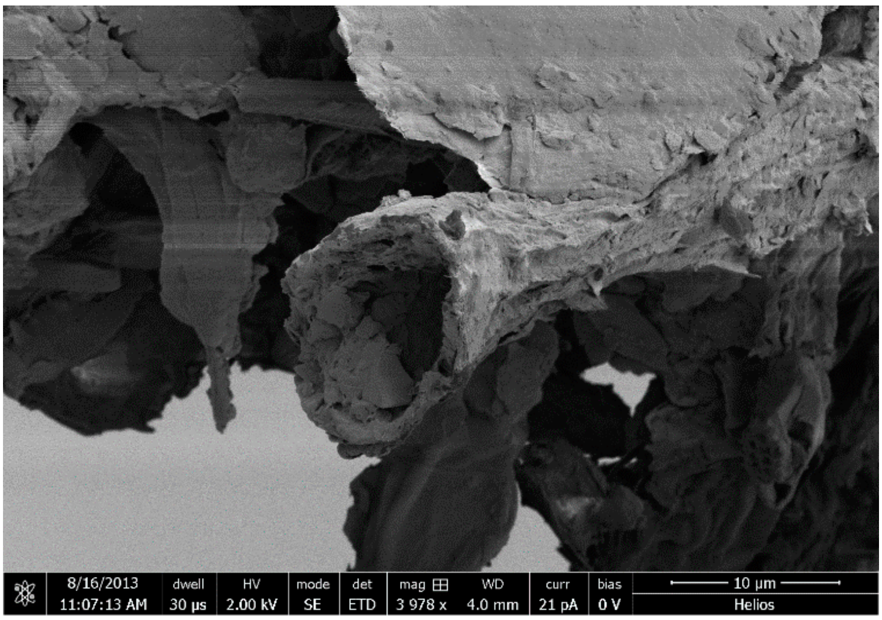

Figure 3. SEM image of the broken stalk of *D. geminata* clearly shows its tubular structure.

Wound healing is another potential use for a *D. geminata* stalk due to its unique sulfated polysaccharide composition. Recent studies have shown that sulfated polysaccharides from seaweeds are harvested and studied as promising sources of wound dressings due to their intrinsic biological activity [28]. Ideally, a wound dressing must be from an inexhaustible source, have the potential for low toxicity, be hypoallergenic, and have the potential for bacterial drug resistance [29]. *D. geminata* stalks are, in theory, a good contender for this application. They also exhibit antioxidant properties, which can be used to prevent the spread of disease [19]. Due to the physical properties of the *D. geminata* stalks, they can be easily pressed into a felt-like banding material. The capillary properties of such a material should determine its effectiveness in relation to blood, plasma, and other biological fluids [30]. Therefore, based on the well-known thermostability of polysaccharide-based materials, it is suggested that there should not be any issues with sterilizations of such kinds regarding *D. geminata*-based wound-dressing materials [31].

The recent pandemic has also been an eye-opener to the extent of our abilities to protect ourselves from deadly viruses. Climate change is also causing more health issues within communities that were previously not known to be vulnerable [32]. With its use in therapeutic purposes within the nutraceutical and pharmaceutical industries, *D. geminata* could have potential uses in the treatment of diseases such as COVID-19 as a filler for corresponding drugs.

Additionally, the authors agree that much work needs to be done to better understand *D. geminata*'s proficiency as a biomaterial. One could also utilize the services of the genome-splicing software 'CRISPR' to induce specific modifications at the genome level that would allow *D. geminata* to function in a more prolific manner as a naturally occurring large-scale biological material. A list of the references corresponding to the biomedical applications of *D.geminata* is provided here (Table 1). This information will help to easily find the reports of biomedical applications in the literature.

Table 1. References corresponding to the different applications of *D. geminata* as a biomaterial.

Applications of *D. geminata* as a Biomaterial	References
Cell Adhesion	[18,22,24,29]
Cell Proliferation	[18,24,29]
Drug Delivery	[2,6,18,19,23,25,29,30]
Wound Dressing	[18,28,29]

3. *D. geminata* Applications in Wastewater Treatment

The composition and structure of *D. geminata*, in particular its multiphase-biomineralized polysaccharide stalks [33], allow for potential valuable applications in wastewater treatment due to its metal-adsorption capacities [34]. The use of microalgae in wastewater treatment is not a novel concept, and research has revealed numerous advantages, such as low cost, high metal-ion uptake, and excellent metal selectivity [35]. Due to the availability of *D. geminata* in various regions, recent studies have emerged investigating the feasibility of using its biomass for heavy-metal remediation in water treatment [4,17]. Polysaccharide-containing biomass, which makes up the extracellular stalks of *D. geminata*, is considered to be an excellent adsorbent of heavy metals, predominantly via functional groups [34]. Wysokowski et al. [34] found that purified *D. geminata* stalks had considerable adsorption capabilities for both nickel(II) and cadmium(II) ions but were especially efficient in the adsorption of lead(II) ions, with a maximum adsorption capacity of 175.48 mg g^{-1} [4,34]. This Pb(II)-adsorption capacity is quite high in comparison to other microalgae biosorbents and, in fact, is almost comparable to the metal-sorption capabilities of some macroalgae (Table 2) [4,17,35,36]. The use of *D. geminata* for heavy-metal adsorption would be especially advantageous in treating industrial wastewater that has been contaminated with lead, which is a priority pollutant associated with high toxicity [37]. There is also potential for *D. geminata* stalks to act as an adsorbent for U(V) ions, with preliminary results showing a 96% decrease in U(V) concentration from adsorption via *D. geminata* nonwoven fabric [25].

Table 2. Pb(II)-sorption capacities for various micro- and macroalgae species.

	Algae Species	Pb(II) Sorption Capacity (mg g^{-1})	Original Reference
Microalgae	*Didymosphenia geminata*	129–175.48	[4,17]
	Chaetoceros sp.	8	[38]
	Chlorella sp.	10.4	[38]
	Phormidium sp.	2.3	[39]
	Rhizoclonium hookeri	81.7	[40]
Macroalgae	*Spirogyra* sp.	140	[41]
	Cladophora fascicularis	198.5	[42]
	Ascophyllum nodosum	178.6	[43]
	Fucus vesiculosus	215.5–259	[44]

Utilizing nonliving *D. geminata* biomass for heavy-metal remediation in water treatment has also proven to be advantageous in terms of sorbent regeneration and reusability [17,45]. Although dried *D. geminata* stalks appear to decrease in mechanical resistance upon adsorption of metals, Wysokowski et al. demonstrated the potential for the material still to go through multiple adsorption and desorption phases, with only a slight decrease in uptake capacity [4,46]. Reinoso-Guerra et al. [17] incorporated *D. geminata* biomass into a nanofibrillated cellulose membrane matrix with the addition of carbon nanotubes (CNTs) to reinforce the material and improve usability in wastewater applications. After evaluating the Pb(II)-adsorption ability of the matrix, it was discovered that the addition of CNTs improved the reusability of the membrane, with increased adsorption and decreased desorption in successive cycles. The boosted adsorption from CNT addition is associated with the enhanced porosity of the membrane and the additional available active sites [17]. Additionally, the presence of CNTs improved the mechanical resistance and antibacterial properties of the *D. geminata* membrane, making the material more viable and economical for water-treatment applications [17].

There is evidence to suggest that the presence of sulfur-based functional groups on *D. geminata* stalks specifically contributes to the excellent adsorption capabilities of the biomaterial [4,17]. The presence of either sulfate esters or sulfonic groups on the isolated polysaccharide stalks has been confirmed through infrared spectroscopy [19]. Metal adsorption on *D. geminata* stalks is thought to occur via a complex mechanism based on ion exchange between hydroxyl and sulfur-based functional groups and metal ions, forming complex ions and coordination bonds (Figure 4) [4,17]. In particular, Reinoso-Guerra et al. directly connected the adsorption of Pb(II) on a *D. geminata* stalk to sulfur-based functional groups through energy-dispersive X-ray spectroscopy (EDS) analysis [17]. Furthermore, experimentally determined maximum adsorption capacities at pH levels between 4 and 6 agree with the dissociation of these sulfur-based functional groups [4,17].

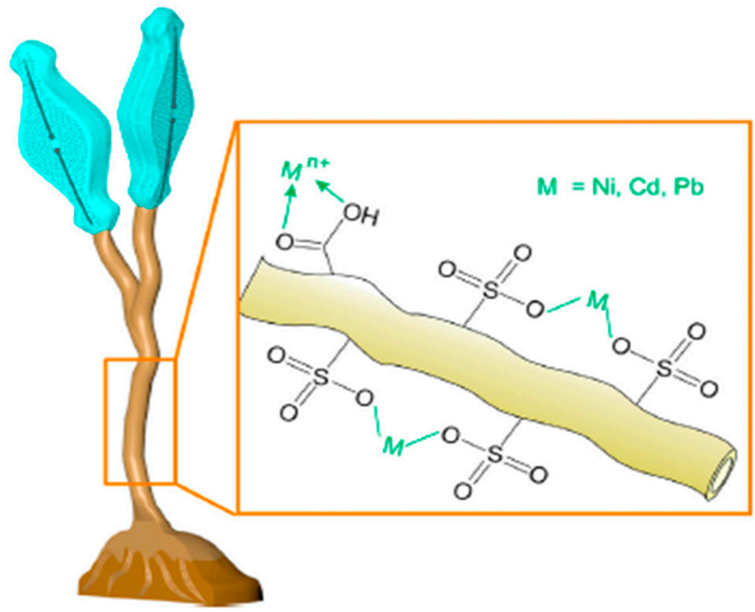

Figure 4. Schematic diagram for the adsorption of metal ions on *D. geminata* stalks [4]. The adsorption mechanism is based on ion exchange between groups on the adsorbent surface (hydroxyl and sulfonic groups) and metal ions, leading to the formation of coordination bonds, as one might observe in the diagram.

4. Environmental Regulations and Policies Pertaining to *D. geminata*

The containment and management of an invasive species requires effective environmental regulations, collaboration between stakeholders, and widespread educational initiatives. In the context of environmental management, it is recommended to focus predominantly on the impacts of a species on its surroundings instead of the geographical origin of the species [47]. Given the growing detrimental effects of *D. geminata*, local authorities have taken steps to contain this species.

Within Canada, to control the spread of *D. geminata*, the Government of Quebec recommends maintaining boats, clothing, and equipment in one waterway when possible [48]. If multiple waterways must be utilized, such items should be cleaned prior to relocation [48]. The Government of Quebec (2008) recommends guidelines developed in New Zealand [48]. Such cleaning protocols include treatment with dishwashing detergent, bleach, hot water, and freezing equipment [49]. Taylor and Bothwell (2014) argued that the current management practices and policies pertaining to decontamination efforts will not be effective in containing *D. geminata*. Instead, the researchers believe the focus should be redirected to identifying which environmental factors/conditions facilitate the spread and bloom of this species [8]. Stalk production for these algae proliferates under low nutrient conditions with a high amount of light [16]. Research by Kilroy and Bothwell (2012) has specifically demonstrated the impact of phosphorus levels on *D. geminata* [50]. Based on this information, local environmental policies should be developed to identify potential environmental areas that may be suitable for the spread of *D. geminata*. Such information can aid conservation authorities in selecting key areas to actively monitor. Credit Valley Conservation has categorized *D. geminata* as an aquatic species on their “watch list” of potentially invasive species [51]. With the aid of the public, conservation authorities should continually monitor areas within their jurisdiction for the emergence of these algae.

Further policy development in this area should focus on providing enhanced educational resources for the public and relevant stakeholders (e.g., outdoor organizations). The government of New Brunswick has recommended improved education efforts for the containment of *D. geminata* [52]. Educational posters and infographics pertaining to *D. geminata* (i.e., cleaning protocols) should be well distributed in priority areas such as locations with increasing blooms. Individuals are encouraged to report sightings of these algae to local authorities [53].

Although *D. geminata* has been labeled invasive, it is important to recognize its potential beneficial applications for biotechnology and biomaterials. We have discussed these fruitful applications throughout this paper. To improve research efforts, scientists should obtain permits for working with this invasive species. Specifically, strict protocols must be implemented to ensure that the species is contained. Researchers and conservation authorities should work collectively to isolate samples of *D. geminata* without any contamination. Leakproof containers must be utilized when transporting the collected samples. Such samples must only be handled in a certified and contained lab setting and discarded appropriately. Furthermore, legal repercussions can assist in ensuring effective compliance. In a global context, New Zealand has taken concrete legal action and has labeled its South Island as a controlled area for these algae [49]. Consequently, individuals are legally obligated to follow outlined cleaning guidelines before changing waterways to ensure that South Island remains free of *D. geminata* [49]. Following New Zealand's initiatives, provinces managing this invasive species should establish specific policies/laws that ensure effective enforcement. Such policies should accommodate research efforts by permitting scientists to work on this species in an isolated setting.

Collectively, the management of *D. geminata* must be implemented via effective environmental regulations, coordination between stakeholders, and enhanced education. Current efforts have focused on implementing cleaning protocols to contain these algae. Alongside such measures, future efforts should also accommodate researchers currently working on invasive species.

5. *D. geminata*'s Economic Impacts

Taking advantage of algae species such as *D. geminata* in industrial practices could be advantageous in reducing the negative impact of invasive species while reusing them as sustainable and natural resources. As mentioned in our previous review [6], *D. geminata*'s ability to treat wastewater and transform it into agricultural fertilizers could bring great economic benefits with its usage; however, it has yet to be determined whether the accompanying side effects of *D. geminata* application would potentially suppress the profitability of the water area. Thus, considerations of its negative impact and growth-controlling plans should be made before *D. geminata* application.

While the commercial impact of *D. geminata* is unknown, studies that investigate the adverse effects of various existing aquatic invasive species (AISs) that are brought to fisheries could be referenced. A report analyzing the economic impact of an AIS on the industries of the Great Lakes states of the U.S. by Rosaen et al. summarized some of the major profit losses by invasive species involving tourism [54]. This nonmarketed loss that is largely due to the rapid spread of AIS can be the result of one of three phenomena: direct operational cost, reduced demand, or decreased productivity. The prevention of AIS spreading requires regular maintenance, which includes but is not limited to water-pipe scraping and chemical treatment. Recreational boating and commercial fishing companies have always relied on the diverse fish species of the local water area. Direct competition within the same habitat due to the occupation of space by AIS can lead to lowered fish stocks and even the extinction of certain species. In addition to the loss of fish population and diversity, the overall demand for tourism can be impacted in several ways. Common examples of reduced customer interest could be that the quality of fish, either its size or health, can no longer meet the expectation of the recreationists, or that beach areas are being occupied with dead fish and fermented rotten algae. Most businesses faced major difficulties opening up, and less-established companies were challenged with permanent shutdown. A reported annual loss of $50 million was due to the reduced demand for businesses and tourism alone [55].

New Zealand, one of the most chronically infected areas, paid an economic cost of $158 million in the first eight years post-*D. geminata* discovery without government intervention [21]. Even with a continuous investment in *D. geminata* control efforts, the preventions themselves could be a nuisance to some of the local businesses. One case study performed in New Zealand focused on the nonmarketed impact that *D. geminata* has on recreational angling industries. AIS management is often extremely complex, with most situations requiring rapid responses to efficiently limit the spread; for one reason, AIS directly competes for the same habitat as some of the most demanded fish species. As reported by Bergey et al., *D. geminata* blooms are observed to thrive in rocky and low-nutrient cold-water streams that are ideal for trout populations [56]. The immediate closure of some of the most demanded trout-fishing streams, regardless of their state of *D. geminata* infection, cost more than it would have to remain open at the time of this study. As a result of the decreased angling accessibility due to mainstem river closure, the fishing effort is thus transferred to smaller stems, threatening the vulnerable fish stock.

It is important to note that the occurrence of *D. geminata* in New Zealand should be considered a special case and not a common situation found in rivers of other regions. In Canada, a study done in 2008 reported that due to the distinct climate in Quebec, salmon rivers are not as impacted as in regions such as the Great Lakes and New Zealand [21]. In addition, studies done on *D. geminata*'s impact on salmon production in British Columbia showed no significance, and some infested rivers of Vancouver were even observed to have huge improvements due to possible natural control mechanisms [48], although *D. geminata* has not yet become a major threat to Canadian fish rivers. However, Canada has endured a reported total of $5.5 billion loss due to the indirect economic burden and the direct management cost from the 16 recognized species [57]. Given the above, the impact of *D. geminata* should still be studied in depth and closely monitored when applying it to the suggested purposes mentioned in this paper.

6. Concluding Remarks

While *D. geminata* can have negative implications on its surrounding environment, due to the specificity of the structural organization of its biosilica-based cell walls as well as polysaccharide stalks it can also offer many positive applications as a unique large-scale source of naturally prestructured functional biological materials. Subsequently, these potential applications extend to both the individual and to the environment. *D. geminata* has the ability to act as a biomaterial for the purposes of cell adhesion, proliferation, drug delivery, and wound healing. Furthermore, it has been demonstrated that the stalks of *D. geminata* have significant adsorption capabilities regarding heavy metals such as lead, nickel, and cadmium, which is particularly promising for heavy-metal remediation in wastewater treatment. To ensure that the extrication of the potential benefits of *D. geminata* does not lead to unwanted spread, it is important that researchers obtain a permit when working with *D. geminata*, that they collaborate with conservation authorities when isolating samples of this species, and that the handling of the samples is only in a certified and contained lab setting. Although past studies have shown that the spread of *D. geminata* has not negatively impacted the salmon population in Canada, proper adherence to protocols is especially important to ensure that Canada is not negatively impacted on an economic level by this species. Overall, *D. geminata* has demonstrated immense potential for use within society under proper guidance.

Author Contributions: Conceptualization, M.A.R.; validation, M.A.R. and H.E.; writing—original draft preparation, M.A.R., E.S., R.S., G.S., N.R. and T.G.; writing—review and editing, M.A.R. and H.E.; supervision, M.A.R.; project administration, M.A.R.; funding acquisition, M.A.R. and H.E. All authors have read and agreed to the published version of the manuscript.

Funding: MAR was supported by the Youth Employment Program (project # 018020008), the Ministry of Employment and Social Development, and Innovation Assistant Program of IRAP-NRC (Project # 967148), Govt. of Canada. HE was partially supported by OPUS 19 grant from the National Science Centre, Poland (2020/37/B/ST5/01909) and by Alexander von Humboldt Polish Honorary Research Scholarship (FNP, Poland).

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: Not applicable.

Conflicts of Interest: The authors declare no conflict of interest.

References

1. Whitton, B.A.; Ellwood, N.T.W.; Kawecka, B. Biology of the Freshwater Diatom Didymosphenia: A Review. *Hydrobiologia* **2009**, *630*, 1–37. [CrossRef]
2. Hussein, H.A.; Abdullah, M.A. Anticancer Compounds Derived from Marine Diatoms. *Mar. Drugs* **2020**, *18*, 356. [CrossRef]
3. Sundareshwar, P.V.; Upadhayay, S.; Abessa, M.; Honomichl, S.; Berdanier, B.; Spaulding, S.A.; Sandvik, C.; Trennepohl, A. *Didymosphenia geminata*: Algal Blooms in Oligotrophic Streams and Rivers. *Geophys. Res. Lett.* **2011**, *38*. [CrossRef]
4. Wysokowski, M.; Bartczak, P.; Żółtowska-Aksamitowska, S.; Chudzińska, A.; Piasecki, A.; Langer, E.; Bazhenov, V.V.; Petrenko, I.; Noga, T.; Stelling, A.L.; et al. Adhesive Stalks of Diatom *Didymosphenia geminata* as a Novel Biological Adsorbent for Hazardous Metals Removal. *CLEAN-Soil Air Water* **2017**, *45*, 1600678. [CrossRef]
5. Ladrera, R.; Gomà, J.; Prat, N. Effects of *Didymosphenia geminata* Massive Growth on Stream Communities: Smaller Organisms and Simplified Food Web Structure. *PLoS ONE* **2018**, *13*, e0193545. [CrossRef]
6. Ejaz, H.; Somanader, E.; Dave, U.; Ehrlich, H.; Rahman, M.A. Didymo and Its Polysaccharide Stalks: Beneficial to the Environment or Not? *Polysaccharides* **2021**, *2*, 69–79. [CrossRef]
7. Elwell, L.C.; Gillis, C.-A.; Kunza, L.A.; Modley, M.D. Management Challenges of *Didymosphenia geminata*. *Diatom Res.* **2014**, *29*, 303–305. [CrossRef]
8. Taylor, B.W.; Bothwell, M.L. The Origin of Invasive Microorganisms Matters for Science, Policy, and Management: The Case of *Didymosphenia geminata*. *Bioscience* **2014**, *64*, 531–538. [CrossRef]
9. Wustmann, M.; Poulsen, N.; Kröger, N.; van Pée, K.-H. Chitin Synthase Localization in the Diatom Thalassiosira Pseudonana. *BMC Mater.* **2020**, *2*, 10. [CrossRef]
10. Brunner, E.; Richthammer, P.; Ehrlich, H.; Paasch, S.; Simon, P.; Ueberlein, S.; van Pée, K.-H. Chitin-Based Organic Networks: An Integral Part of Cell Wall Biosilica in the Diatom Thalassiosira Pseudonana. *Angew. Chem. Int. Ed.* **2009**, *48*, 9724–9727. [CrossRef]
11. Zgłobicka, I.; Li, Q.; Gluch, J.; Płocińska, M.; Noga, T.; Dobosz, R.; Szoszkiewicz, R.; Witkowski, A.; Zschech, E.; Kurzydłowski, K.J. Visualization of the Internal Structure of *Didymosphenia geminata* Frustules Using Nano X-ray Tomography. *Sci. Rep.* **2017**, *7*, 9086. [CrossRef]
12. Brand, C.; Grech, M. Recent Invasion of *Didymosphenia geminata* (Lyngbye) M. Schmidt in a Patagonian Regulated River Promotes Changes in Composition and Density of Macroinvertebrate Community. *Biol. Invasions* **2020**, *22*, 1903–1915. [CrossRef]
13. Jellyman, P.G.; Harding, J.S. Disentangling the Stream Community Impacts of *Didymosphenia geminata*: How Are Higher Trophic Levels Affected? *Biol. Invasions* **2016**, *18*, 3419–3435. [CrossRef]
14. Jones, L.R.; Manrique, J.M.; Uyua, N.M.; Whitton, B.A. Genetic Analysis of the Invasive Alga *Didymosphenia geminata* in Southern Argentina: Evidence of a Pleistocene Origin of Local Lineages. *Sci. Rep.* **2019**, *9*, 18706. [CrossRef] [PubMed]
15. Bothwell, M.L.; Taylor, B.W.; Kilroy, C. The Didymo Story: The Role of Low Dissolved Phosphorus in the Formation of *Didymosphenia geminata* Blooms. *Diatom Res.* **2014**, *29*, 229–236. [CrossRef]
16. Kilroy, C.; Bothwell, M. Environmental Control of Stalk Length in the Bloom-Forming, Freshwater Benthic Diatom *Didymosphenia geminata* (Bacillariophyceae). *J. Phycol.* **2011**, *47*, 981–989. [CrossRef]
17. Reinoso-Guerra, E.; Aristizabal, J.; Arce, B.; Zurob, E.; Dennett, G.; Fuentes, R.; Suescún, A.V.; Cárdenas, L.; da Cunha, T.H.R.; Cabezas, R.; et al. Nanostructured *Didymosphenia geminata*-Based Membrane for Efficient Lead Adsorption from Aqueous Solution. *J. Environ. Chem. Eng.* **2021**, *9*, 105269. [CrossRef]
18. Wahab, I.F.; Razak, S.I. Polysaccharides as Composite Biomaterials. In *Composites from Renewable and Sustainable Materials*; InteahOpen: London, UK, 2016; pp. 65–84. [CrossRef]
19. Figueroa, F.A.; Abdala-Díaz, R.; Hernández, V.; Pedreros, P.; Aranda, M.; Cabrera-Pardo, J.R.; Pérez, C.; Becerra, J.; Urrutia, R. Invasive Diatom *Didymosphenia geminata* as a Source of Polysaccharides with Antioxidant and Immunomodulatory Effects on Macrophage Cell Lines. *J. Appl. Phycol.* **2020**, *32*, 93–102. [CrossRef]
20. Williams, D.F. On the Nature of Biomaterials. *Biomaterials* **2009**, *30*, 5897–5909. [CrossRef] [PubMed]
21. Bothwell, M.L.; Spaulding, S.A. Synopsis of the 2007 International Workshop on *Didymosphenia geminate*. In *Proceedings of the 2007 International Workshop on Didymosphenia geminate*; Fisheries and Oceans Canada: Ottawa, ON, Canada, 2008; 96p.
22. Zgłobicka, I. Aspects of Structural Biology of *Didymosphenia geminata* (Lyngb.) M. Schmidt (*Bacillariophyta*). *IJA* **2013**, *15*, 291–310. [CrossRef]
23. Zglobicka, I. Frustules of *Didymosphenia geminata* as a Modifier of Resins. *Mater. Eng.* **2018**, *1*, 10–16. [CrossRef]
24. Arora, M.; Arora, E. The Promise of Silicon: Bone Regeneration and Increased Bone Density. *J. Arthrosc. Jt. Surg.* **2017**, *4*, 103–105. [CrossRef]
25. Zgłobicka, I. Exploratory Study of the Use of *Didymosphenia geminata* Stalks as a Functional Biomaterial. Ph.D. Thesis, Division of Materials Design, The Warsaw University of Technology, Warszawa, Poland, 2015.

26. Wang, N.; Cheng, X.; Li, N.; Wang, H.; Chen, H. Nanocarriers and their loading strategies. *Adv. Healthc. Mater.* **2019**, *8*, 1801002. [CrossRef] [PubMed]
27. Przekora, A. The Summary of the Most Important Cell-Biomaterial Interactions That Need to Be Considered during in Vitro Biocompatibility Testing of Bone Scaffolds for Tissue Engineering Applications. *Mater. Sci. Eng. C* **2019**, *97*, 1036–1051. [CrossRef]
28. Andryukov, B.G.; Besednova, N.N.; Kuznetsova, T.A.; Zaporozhets, T.S.; Ermakova, S.P.; Zvyagintseva, T.N.; Chingizova, E.A.; Gazha, A.K.; Smolina, T.P. Sulfated Polysaccharides from Marine Algae as a Basis of Modern Biotechnologies for Creating Wound Dressings: Current Achievements and Future Prospects. *Biomedicines* **2020**, *8*, 301. [CrossRef]
29. Kuznetsova, T.A.; Andryukov, B.G.; Besednova, N.N.; Zaporozhets, T.S.; Kalinin, A.V. Marine Algae Polysaccharides as Basis for Wound Dressings, Drug Delivery, and Tissue Engineering: A Review. *J. Mar. Sci. Eng.* **2020**, *8*, 481. [CrossRef]
30. Medarević, Đ.; Losić, D.; Ibrić, S. Diatoms—Nature materials with great potential for bioapplications. *Hem. Ind.* **2016**, *70*, 613–627. [CrossRef]
31. Marreco, P.R.; Moreira, P.D.L.; Genari, S.C.; Moraes, Â.M. Effects of different sterilization methods on the morphology, mechanical properties, and cytotoxicity of chitosan membranes used as wound dressings. *J. Biomed. Mater. Res.* **2004**, *71*, 268–277. [CrossRef]
32. Ebi, K.L.; Hess, J.J. Health Risks Due to Climate Change: Inequity in Causes and Consequences. *Health Aff.* **2020**, *39*, 2056–2062. [CrossRef]
33. Ehrlich, H.; Motylenko, M.; Sundareshwar, P.V.; Ereskovsky, A.; Zgłobicka, I.; Noga, T.; Płociński, T.; Tsurkan, M.V.; Wyroba, E.; Suski, S.; et al. Multiphase Biomineralization: Enigmatic Invasive Siliceous Diatoms Produce Crystalline Calcite. *Adv. Funct. Mater.* **2016**, *26*, 2503–2510. [CrossRef]
34. Na, Y.; Lee, J.; Lee, S.H.; Kumar, P.; Kim, J.H.; Patel, R. Removal of Heavy Metals by Polysaccharide: A Review. *Polym.-Plast. Technol. Mater.* **2020**, *59*, 1770–1790. [CrossRef]
35. Zeraatkar, A.K.; Ahmadzadeh, H.; Talebi, A.F.; Moheimani, N.R.; McHenry, M.P. Potential Use of Algae for Heavy Metal Bioremediation, a Critical Review. *J. Environ. Manag.* **2016**, *181*, 817–831. [CrossRef]
36. Ubando, A.T.; Africa, A.D.M.; Maniquiz-Redillas, M.C.; Culaba, A.B.; Chen, W.-H.; Chang, J.-S. Microalgal Biosorption of Heavy Metals: A Comprehensive Bibliometric Review. *J. Hazard. Mater.* **2021**, *402*, 123431. [CrossRef] [PubMed]
37. Arbabi, M.; Hemati, S.; Amiri, M. Removal of Lead Ions from Industrial Wastewater: A Review of Removal Methods. *Int. J. Epidemiol. Res.* **2015**, *2*, 105–109.
38. Molazadeh, P.; Khanjani, N.; Rahimi, M.; Nasiri, A. Adsorption of lead by microalgae *Chaetoceros* sp. and *Chlorella* sp. from aqueous solution. *J. Community Health Res.* **2015**, *4*, 114–127.
39. Das, D.; Chakraborty, S.; Bhattacharjee, C.; Chowdhury, R. Biosorption of Lead Ions (Pb^{2+}) from Simulated Wastewater Using Residual Biomass of Microalgae. *Desalination Water Treat.* **2016**, *57*, 4576–4586. [CrossRef]
40. Suganya, S.; Saravanan, A.; Senthil Kumar, P.; Yashwanthraj, M.; Sundar Rajan, P.; Kayalvizhi, K. Sequestration of Pb (II) and Ni (II) Ions from Aqueous Solution Using Microalga *Rhizoclonium hookeri*: Adsorption Thermodynamics, Kinetics, and Equilibrium Studies. *J. Water Reuse Desalination* **2016**, *7*, 214–227. [CrossRef]
41. Gupta, V.K.; Rastogi, A. Biosorption of Lead from Aqueous Solutions by Green Algae Spirogyra Species: Kinetics and Equilibrium Studies. *J. Hazard. Mater.* **2008**, *152*, 407–414. [CrossRef] [PubMed]
42. Deng, L.; Su, Y.; Su, H.; Wang, X.; Zhu, X. Sorption and Desorption of Lead (II) from Wastewater by Green Algae *Cladophora fascicularis*. *J. Hazard. Mater.* **2007**, *143*, 220–225. [CrossRef]
43. Romera, E.; González, F.; Ballester, A.; Blázquez, M.L.; Muñoz, J.A. Comparative Study of Biosorption of Heavy Metals Using Different Types of Algae. *Bioresour. Technol.* **2007**, *98*, 3344–3353. [CrossRef]
44. Rincón, J.; González, F.; Ballester, A.; Blázquez, M.; Muñoz, J. Biosorption of Heavy Metals by Chemically Activated Alga *Fucus vesiculosus*. *J. Chem. Technol. Biotechnol.* **2005**, *80*, 1403–1407. [CrossRef]
45. Pavithra, K.G.; Kumar, P.S.; Jaikumar, V.; Vardhan, K.H.; SundarRajan, P. Microalgae for Biofuel Production and Removal of Heavy Metals: A Review. *Environ. Chem. Lett.* **2020**, *18*, 1905–1923. [CrossRef]
46. Zgłobicka, I.; Chlanda, A.; Woźniak, M.; Łojkowski, M.; Szoszkiewicz, R.; Mazurkiewicz-Pawlicka, M.; Święszkowski, W.; Wyroba, E.; Kurzydłowski, K.J. Microstructure and Nanomechanical Properties of Single Stalks from Diatom *Didymosphenia geminata* and Their Change Due to Adsorption of Selected Metal Ions. *J. Phycol.* **2017**, *53*, 880–888. [CrossRef] [PubMed]
47. Davis, M.A.; Chew, M.K.; Hobbs, R.J.; Lugo, A.E.; Ewel, J.J.; Vermeij, G.J.; Brown, J.H.; Rosenzweig, M.L.; Gardener, M.R.; Carroll, S.P.; et al. Do not Judge Species on Their Origins. *Nature* **2011**, *474*, 153–154. [CrossRef] [PubMed]
48. Ministère du Développement Durable, de L'environnement et des Parcs; Ministère des Ressources Naturelles et de la Faune. *What Is Didymo and How Can We Prevent It from Spreading in Our Rivers?* Ministère du Développement Durable, de l'Environnement et des Parcs: Rouyn-Noranda, QC, Canada, 2008; 13p.
49. Ministry of Primary Industries. Check, Clean, Dry: Preventing Didymo and Other Pests. Available online: https://www.mpi.govt.nz/outdoor-activities/boating-and-watersports-tips-to-prevent-spread-of-pests/check-clean-dry/ (accessed on 27 October 2021).
50. Kilroy, C.; Bothwell, M.L. *Didymosphenia geminata* Growth Rates and Bloom Formation in Relation to Ambient Dissolved Phosphorus Concentration. *Freshw. Biol.* **2012**, *57*, 641–653. [CrossRef]
51. Credit Valley Conservation. CVC Priority Aquatic Invasive Species & Fish Diseases. 2009. Available online: https://cvc.ca/wp-content/uploads/2011/02/CVC_AquaticInvasives_FishDiseases1.pdf (accessed on 15 August 2021).

52. Government of New Brunswick Canada. *Didymosphenia geminate*. Available online: https://www2.gnb.ca/content/gnb/en/departments/erd/natural_resources/content/fish/content/Didymo.html (accessed on 24 October 2021).
53. Government of Saskatchewan. Didymo Rock Snot Fact Sheet. Available online: http://www.environment.gov.sk.ca/Default.aspx?DN=e1c161fd-0a5c-4804-8296-0709df01300d (accessed on 27 October 2021).
54. Rosaen, A.L.; Grover, E.A.; Spencer, C.W. *The Costs of Aquatic Invasive Species to Great Lakes States*; Anderson Economic Group: East Lansing, MI, USA, 2016; 51p.
55. Beville, S.T.; Kerr, G.N.; Hughey, K.F.D. Valuing Impacts of the Invasive Alga *Didymosphenia geminata* on Recreational Angling. *Ecol. Econ.* **2012**, *82*, 1–10. [CrossRef]
56. Bergey, E.A.; Cooper, J.T.; Phillips, B.C. Substrate Characteristics Affect Colonization by the Bloom-Forming Diatom *Didymosphenia geminata*. *Aquat. Ecol.* **2010**, *44*, 33–40. [CrossRef]
57. Government of Canada, Fisheries and Oceans Canada. A Canadian Action Plan to Address the Threat of Aquatic Invasive Species. Available online: https://www.dfo-mpo.gc.ca/species-especes/publications/ais-eae/plan/page01-eng.html (accessed on 24 October 2021).