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MUSSEL BIOADHESIVES: A TOP LESSON FROM NATURE

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Abstract. *L*-Dopa-containing proteins with adhesive property exist within the mussel feet, commonly called mussel foot proteins (*fp*s). These bioadhesive proteins adhered tightly to all kinds of surfaces and, more interesting, under wet environment. Catechol functionality of Dopa plays crucial role for such adhesion. Mussel-inspired catechol-containing polymers were conceived and their adhesion forces were compared to the commercial glues. Applications in biomedicals, hydrogels, antifoulings, and nanotechnology are claimed. One promising outlook is the surgical suture with such bioadhesive and the engineering of self-healing related materials.

Keywords: adhesive, bioadhesive, catechol, dopa, mussel, polymer

Introduction

Background in chemistry, as with other scientific disciplines, is better acquired in schools, colleges, and universities, providing two essential elements: a chemistry teacher and a laboratory. Observed phenomena in chemical experiments have led to set laws, structures, and properties. The advent of science, in general, has allowed delving into a deeper pit of the matter, developing hence the nanoscience of which emerged the nanochemistry. All the sofar-made discoveries and the upcoming ones are but the already-created phenomena, natural ones, which man has cleverly deciphered. Nature must be understood as the man surroundings including himself (man, animals, plants, trees, oceans, sky, earth, planets, etc.). Chemist has reached a level of scientific maturity to conceive and make molecules of his own, either for a mere curiosity or for a targeted objective. However, natural molecules or commonly called *natural products* stand superior by far *vis-à-vis* the synthetic or man-made ones. For example, it has been demonstrated that the natural vitamins are safer, more effective than the synthetic analogues, and their absorption by the metabolism is somewhat different, although the molecular architectures are wholly identical (Thiel, 2000). Yet, the good side of this event is the daring of chemist to accept the challenge of making the natural molecules of intricate architectures. Examples of such synthesized natural molecules are innumerable and the multistep routes of making them are excitingly onerous (Nicolau et al., 2000).

An ever-leading one is the synthesis of vitamin B12 whose designer or builder was crowned with a Nobel Prize, for achieving such a robust challenge (Moulay, 2007). Total biosynthesis of natural products remains unique, defying, and undecipherable. And, to reproduce and comprehend such natural phenomena may be mere efforts. Natural rubber, a hydrocarbon polymer, is secreted in a form of an emulsion consisting of this polymer in spherical form finely dispersed in aqueous medium that contains several other components (proteins, phospholipids, fats, waxes, aminoacids and other organic acids such ascorbic acid, carbohydrates, sterols, ….etc) in small portions (0.002 to 1%) (Jacob et al., 1993). Synthetic rubber, however, requires a lesser number of different ingredients. Nowadays, even the organic synthesis is being oriented to biological systems, so-called *Green Chemistry*, that is to handle the work-up in environmentally friendly aqueous media, avoiding the use of the toxic organic solvents.

Other spellbinding and impressive species are spiders. Indeed, spiders secrete different natural silks (like dragline silk) for different purposes, whose mechanical properties are rivaling those of engineering polymers such as aramid and Kevlar (Vollrath, 2000; Hinman et al., 2000; Vollrath et al., 2011), and whose adhesive properties are but stunning (Sahni et al., 2011); the spiders' silks are among the toughest materials ever known.

Mussel bioadhesive

Adhesives are materials of a paramount importance in our modern life, facilitating the firm assembly of objects for various applications. The variety of chemical natures of adhesives is closely linked to the different natures of the substrata (organic and inorganic), a fact imposed by the sizing extent. Classical or conventional adhesives are based on natural resins and natural/synthetic polymers, as their solutions stand as colloidal systems: emulsions of some acrylic polymers and poly(vinyl acetate) (Elmer's glue, for paper and wood sizing), ethylcyanoacrylate glue (Krazy glue, for objects of all kinds), epoxy resins/hardener system (Quick-set), and urea- and phenol- formaldehyde resins. The adhesiveness of these materials to items occurred usually under dry (wet out) environment. Their adhesion on water-wetted objects does not happen for water molecules will prevent the attractive forces between the adhesive and bonding surface from taking place. Thus, an adhesive with a property of sticking to a wet substrate would be of a great value and its realization would be certainly of a great accomplishment. While man perceives this adhesive not to be possible, nature masterly approves it. Indeed, and to man's surprise, there exist mollusks called "Mussels" (Fig. 1) whose feet secrete a sticky liquid that allows them to attach to rocks in seawaters. The mussels family is composed of three members, distinct by their colors: *Mytilus edulis* (blue), *Perna viridis* (green), and *Dreissena polymorpha* (zebra). Bioadhesives are also secreted from other animals (insects and reptiles) and plants (Von Byern & Grunwald, 2010; Favi et al., 2014).

Fig. 1. Mussel with its feed attached to the rock

To alleviate such a surprise and quench one's curiosity, several workers succeeded in unraveling the secret behind this gluing phenomenon of mussel in water environment (Waite & Tanzer, 1981; Waite, 1999; 2002; Lin et al., 2007). The outcome is that this bioadhesive substance is of a proteinaceous nature, commonly coined either "mussel adhesive protein" (MAP) or "mussel foot protein" (*Mfp*). A feature of this protein is that its chemical structure bears 3,4-dihydroxypheny-*L*-alanine (Dopa), a natural molecule formed by posttranslational modification of tyrosine, as pictured in Fig.2. The catechol functionality in Dopa, being catecholamine, was found to be primarily responsible for water-resistant adhesion to all substrates (Lee et al., 2006a; Lee et al., 2006b). Five *Mfp*'s were extracted from *Mytilus edulis* species with different molecular weights and different Dopa contents as gathered in Table 1 (Rzepecki & Waite, 1991).

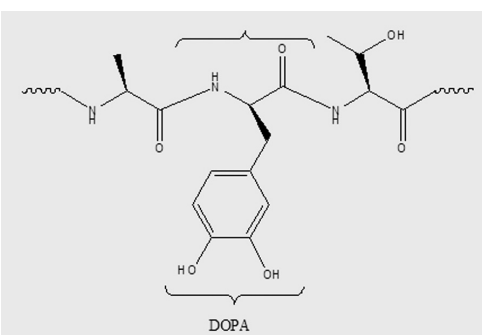

Fig. 2. Chemical structure of mussel foot protein, *Mfp*

Table 1. The different foot proteins from *Mytilus edulis*(Waite, 2002)[1)]

Protein	Molecular weight (g/mol)	Dopa (mol.%)
Mfp-1	110 000	13
Mfp-2	40 000	3
Mfp-3	6 000	20
Mfp-4	80 000	4
Mfp-5	9 000	30

As expected, the actual adhesion on different substrata is better assured by *Mfp*'s of higher Dopa contents. Indeed, while *Mfp*-2 and *Mfp*-4 that are of the lowest Dopa contents and of moderate molecular weights do not show appreciable contribution, *Mfp*-3 and *Mfp*-5 that are of highest DOPA contents and of the lowest molecular weights serve as the adhesive primers, and *Mfp*-1 that is of moderate Dopa content and of the highest molecular weight acts as the coating. This observation is a reminder of the paint coating which requires a primer layer for a better adhesion to the substrate and a coating layer for its protection. Such different roles seem to be linked to the spatial structures of the *Mfp*'s. The mechanism of the adhesion of *Mfp*'s onto wet surfaces was revealed to involve the oxidation of catechol units of Dopa to a certain extent (Rzepecki & Waite, 1991; Petrone, 2013; Bandara et al., 2013) leading to crosslinking by a coupling phenomenon, and the reaction of free amines of the *Mfp*'s with carbonyl groups of the dopaquinones via Michael reaction (Fig.3). However, a balance between cohesive and adhesive bonding interactions is requisite for an optimum adhesion. Lower Dopa oxidation and higher crosslinking extent secure this balance. Besides, polar surfaces undergo greater adhesion than the non-polar ones. *In vivo*, catecholase enzyme promoted the dopaquinone formation in the course of underwater adhesion. Yet, naked catechol functionality, that is the reduced form, implies an adhesion enhancing. Hence, as may be remarked, a clear-cut mechanism in this wet bioadhesiveness seems to be far-reached as several species and sites are involved.

The force or energy of adhesion of mussel foot proteins to several adherends including mica, glass, silica, metals (Au, Ag, Pt, and Pd), metal oxides (Al_2O_3, Cr_2O_3, TiO_2, Ta_2O_5, Nb_2O_5, ZrO_2, Fe_2O_3), quartz, slate, ceramic, wood, skin, and synthetic polymers (PVC,

PS, PMMA, polyurethane, PET, teflon, silicone rubber, etc.) can be experimentally assessed (Moulay, 2014). For example, adhesion energy W_{adh} for joining two mica surfaces with *Mfp*-3 was in the range of 0.03-14mJ/m^2, depending on the pH. The adhesion force, that is the interaction extent between the *Mfp*'s and the surfaces, is tightly linked to the backbone flexibility of proteins and to the chemical nature of the surfaces; the differences in the interaction were imputed to several mechanism including electrostatic, hydrogen bonding, hydrophobic interactions, cation-π interaction, π-π stacking, and metal-complexation.

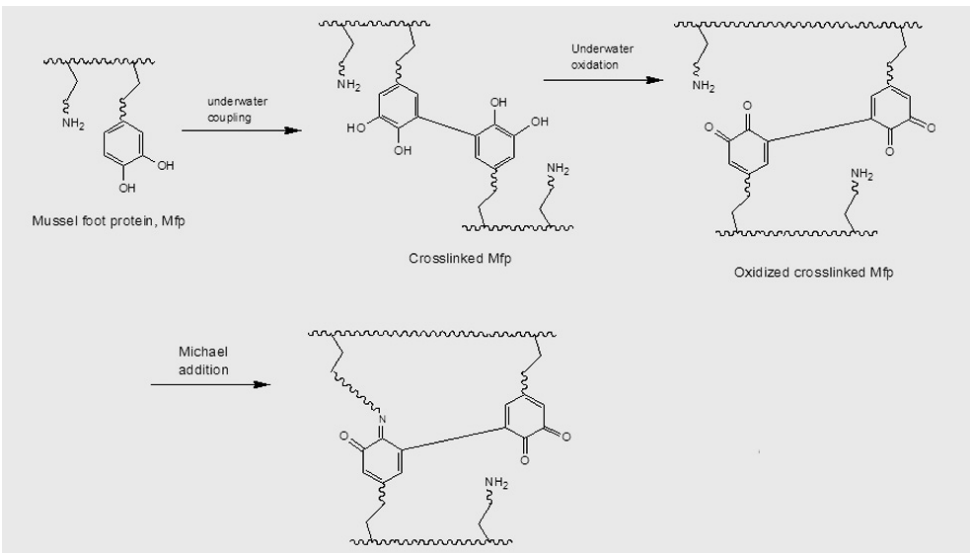

Fig. 3. Reactions involved in the mechanism of the adhesion of *Mfp*'s.

In vitro, crosslinking of the *Mfp*'s shown in Fig.3 during adhesion process could be achieved using several kinds of crosslinkers or crosslinking inducers such as periodate ion (IO_4^-) and cupric ion (Cu^{2+}). The oxidation of catechol unit of Dopa, a transformation that occurs to a certain extent during the adhesion, could occur either by raising the pH of the medium (auto-oxidation) or by using periodate ion acting as an oxidizing agent; the strength of adhesion *Mfp*-3 to mica surface decreased either with increasing pH or when periodate solution was added. Clearly, the dopaquinone formation would lessen the adhesion significantly. *Mfp*-1 proteins, highly positively charged polyelectrolytes and devoid of cohesive tendency, were useless in adhering two mica surfaces but effective when experimented in the presence of low Fe(III) aqueous solution concentrations; this was imputed to the bridging formation between *Mfp*-1 layers, resulting from

iron(III)-catechol units complexation (chelation). In fact, the adhesion energy W_{adh} was measured in the range of 4.3 mJ/m^2, a value greater than that for *Mfp*-3/mica (0.6 mJ/m^2) (Zeng et al., 2010).

Mussel-bioinspired adhesives

As a routine step in research, synthetic chemists put forward the lessons from nature and, without further delay, undertake the conception of *Mfp*-like materials for a better understanding of the Dopa-related adhesiveness. To this end, the basic strategy was either to attach covalently the catechol-containing molecule to a premade polymeric matrix (Fig.4), or to polymerize/copolymerize catechol-bearing monomers or catechol precursor monomers (Fig.5). Yet, stringent requirements for polymeric matrixes and for the latter monomers are to be in tune with coveted adhesive properties and biomimetic *Mfp*'s. For example, PEG is a versatile candidate for catechol functionalization because of its biocompatibility fulfillment, biodegradability, nontoxicity and non-immunogenicity, as required for its bioapplication.

Several polymers, synthetic and natural ones, were subjected to functionalization with catechol-containing molecules. Of these polymers there are hyaluronic acid, chitosan, alginate, cellulose (cotton), poly(ethylene glycol) (PEG), polyethylenimine (PEI), polysiloxanes, poly(ethylene oxide)-poly(propylene oxide)-poly(ethylene oxide) (PEO-PPO-PEO) block copolymers, butadiene and maleic anhydride copolymers, poly(ethylene glycol)-*b*-poly(2-methyl-2-carboxyl-propylene carbonate)-*b*-poly(*L*-lactide), poly(methyl methacrylate)-poly(methacrylic acid)-poly(methyl methacrylate) (PMMA-PMAA-PMMA), poly(acrylic acid), and multi-walled carbon nanotubes (MWCNT). The grafting catechol-containing molecules involved in such functionalization were: Dopa, α-methylDopa, dopamine, α-methyldopamine, norepinephrine, 3,4-dihydroxyphenylpropionic acid, and 3,4-dihydroxyphenylacetic acid. Most importantly is the polymerization/copolymerization of a monomer having catechol/catechol precursor units as pictured in Fig.5. The catecholic monomers and co-monomers comprise the vinylics such as dopamine methacrylamide, *N*-(3,4-dihydroxyphenethyl) methacrylamide, *N*-2-(3′,4′-di-triethylsilyloxyphenyl)ethyl methacrylamide, *N*-dopamine methacrylamide, 3,4-di-trimethylsilyloxystyrene, 3,4-dimethoxystyrene, *N*-methacrylated Dopa, Dopa/catechol-containing macromonomer, and the polyfunctional ones such as Dopa and derivatives, dopamine, norepinephrine, 3,4-dihydroxycinnamic acid, 3,4-dihydroxyhydrocinnamic acid.

For illustrative purpose, some related catechol-containing materials are herein cited. Dopamine-functionalized hyaluronic acid (Fig.6) proved to be efficient in building layer-by-layer (LBL) assembly on several synthetic polymer surfaces (PTFE, PET, PE, PC) (Lee et al., 2008; Messershmith et al., 2012); such assembly was ensured through

the adhesivity of catechol groups. Dopa-functionalized poly(ethylene glycol) (Fig.7) showed good adhesive and mechanical properties upon treatment with Fe(III) solutions (Statz et al., 2006; Holten-Andersen et al., 2011); different catecholato-Fe^{3+} complexes were formed depending on the pH. LBL assembly could be built by chitosan and the conjugate dopamine-modified hyaluronic acid; the adhesion strength of the multilayer film obtained was in the range of 2.30 MPa, a high strength when compared to that for multilayer film made from chitosan and unmodified hyaluronic acid (0.75 MPa) (Neto et al., 2014).

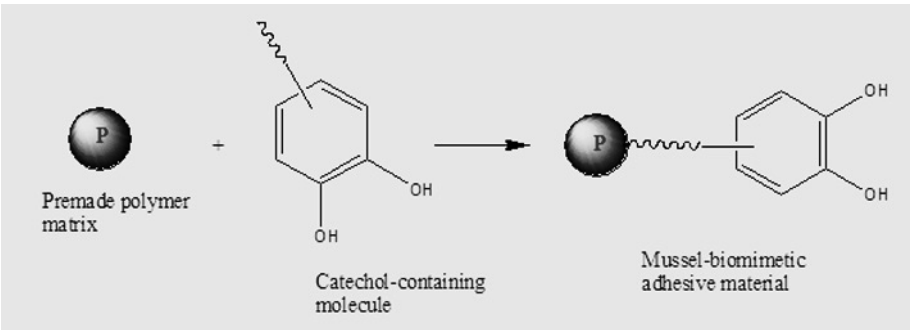

Fig. 4. Biomimetic adhesive material via functionalization of polymer with a catechol-containing molecule

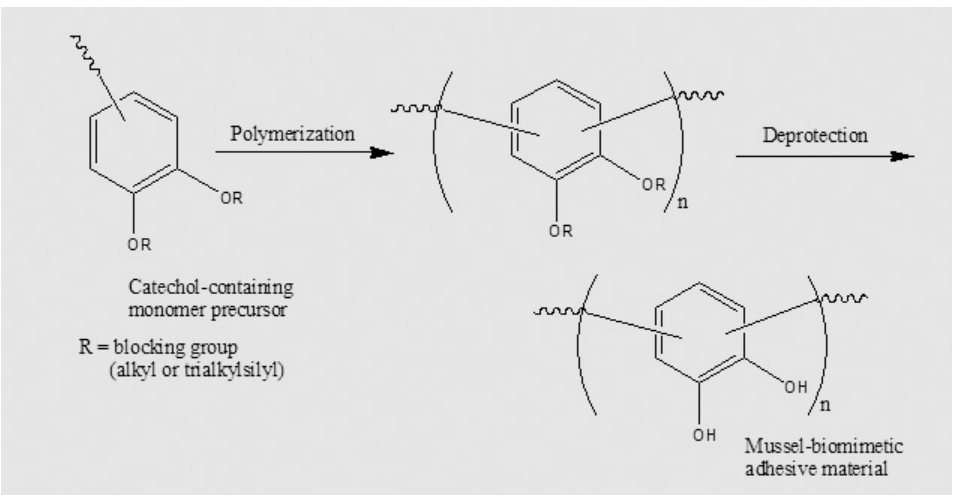

Fig. 5. Biomimetic adhesive material via polymerization of a catechol-containing monomer

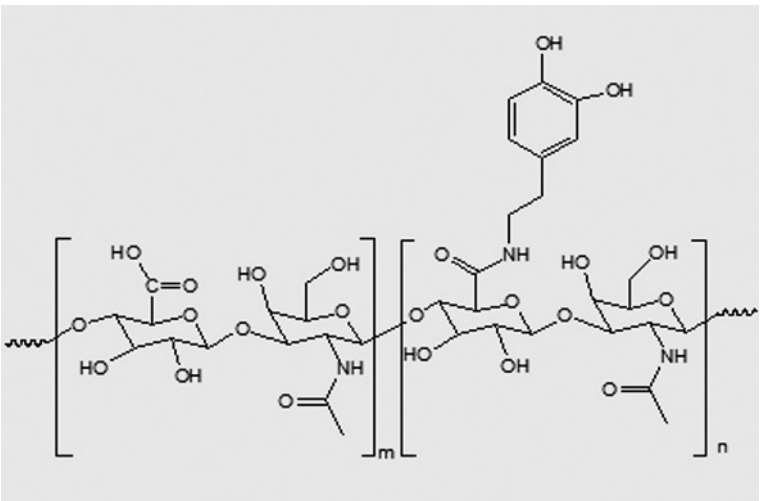

Fig. 6. Dopamine-functionalized hyaluronic acid

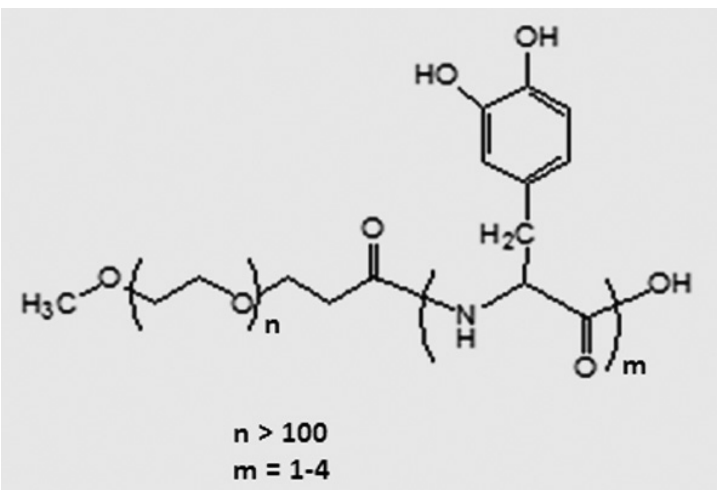

Fig. 7. Dopa-functionalized PEG (either mono- or four-arm PEG)

A bioinspired adhesive could be made by mixing the demethylated lignin (after cellulose, lignin is ranked as a second component of plants) and polyethylenimine (PEI) in aqueous medium at pH = 10 (Liu & Li, 2006); the lap shear strength of the adhesive

applied between two maple veneers attained ~1.5-2 MPa in wet experimental conditions. Materials made by polycondensation of caffeic acid (3,4-dihydroxycinnamic acid) and coumaric acid (4-hydroxycinnamic acid) exhibited an adhesion force, when applied to carbon and glass fibers, of about 7 MPa, a value matching that for superglue (Kaneko et al., 2011). Surface coating could be realized by polymerizing Dopa or dopamine, simply by immersion of the object into buffer solutions (pH = 8.5) of these two monomers, either in Tris-HCl (Tris = 2-amino-2-(hydroxymethyl)propane-1,3-diol) or phosphate buffer solution (PBS) (Na_2HPO_4 + KH_2PO_4) (Xi et al., 2009; Yu et al., 2010; Ku et al., 2010). The polyDopa and polydopamine were believed to have the structure shown in Fig.8, elucidating the catechol functionality that is responsible for coating formation. Poly(3,4-dihydroxystyrene-*co*-styrene) and poly(3,4-dihydroxystyrene-*co*-styrene-*co*-*p*-OEGstyrene) (OEG = oligo(ethylene glycol)) were conceived as biomimetic mussel adhesives and were made by radical copolymerization of 3,4-dimethoxystyrene with styrene (Fig.9) (Westwood et al., 2007; Matos-Pérez et al., 2012; Matos-Pérez & Wilker, 2012; Jenkins et al., 2013; Meredith et al., 2014; Neto et al., 2013). Adhesion of poly(3,4-dihydroxystyrene-*co*-styrene) cured by treatment with oxidants such as Fe^{3+}, IO_4^-, and $Cr_2O_7^{2-}$, onto aluminum substrate was estimated by lap-shear testing and was dependent on the curing agent; that is, for a composition of 3.4:96.6 of 3,4-dihydroxystyrene:styrene copolymer (average molecular weight M_n = 16 150 g/mol), the adhesion strength was 0.7, 0.9, and 1.2 MPa, respectively. Besides, the adhesion propensity is linked to the molecular weight of the copolymer. For a copolymer with molecular weight of M_n = 60 000 g/mol, the lap shear on Al substrate was about 11MPa, and those for commercial glues such as Elmer's glue (polyvinyl acetate), superglue (ethylcyanoacrylate), and quickset glue (epoxy) were 3.8, 5 and 18 MPa, respectively.

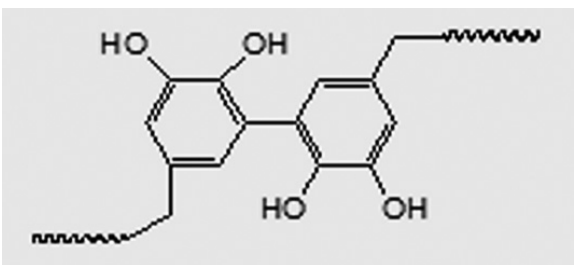

Fig. 8. Proposed structure of polyDopa and polydopamine

Applications and outlook

In parallel with the advent of synthesis of the mussel-mimetic materials, a number of uses and applications have been shortly sighted and prospected, exploiting the valuable adhesiveness property of catechol functionality (Moulay, 2014), profitably in biomedicals (Mehdizadeh & Yang, 2013; Bouten et al., 2014).

Antifouling of microorganisms on wet surfaces such as ship hulls has been always of a primary concern. Thus, the undesirable biofouling could be prevented by applying a mussel-mimicking polymer (Statz et al., 2005; Dalsin & Messersnith, 2005; Yang et al., 2014), such as the one shown in Fig.10, as a coating onto the naked surfaces. The Dopa/catechol-modified PEG materials such as that shown in Fig.7, have an antifouling capacity against marine algae and bacterium when coated on Ti, Si, Au, Al, silicone surfaces, and show a resistance to protein adsorption such as human serum and fibrinogen and to mammalian cells.

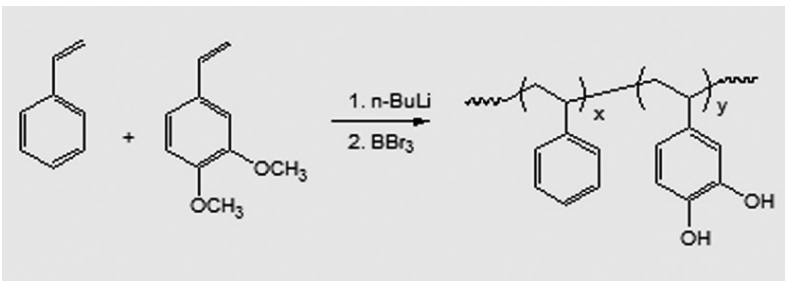

Fig. 9. Synthesis of poly[(3,4-dihydroxystyrene)-*co*-styrene], a mussel-inspired material

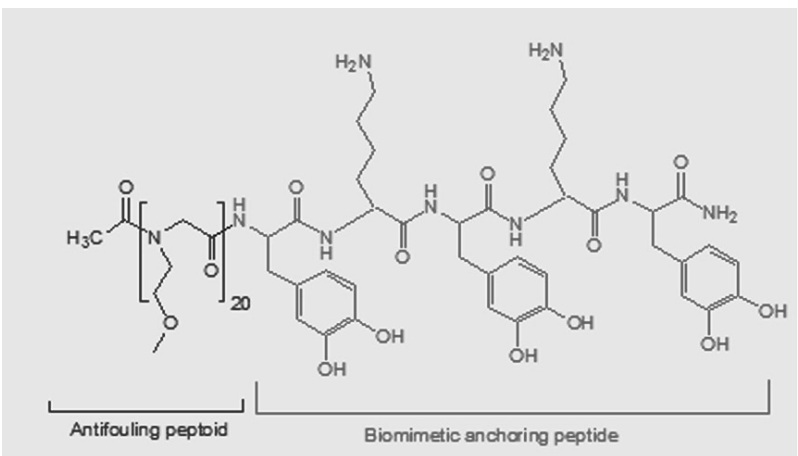

Fig. 10. An antifouling catechol-containing polymer

Needless is to recall the merits of the hydrogels in our today's items such as the biomedicals. Henceforth, the use of mussel-bioinspired polymers in hydrogels making is of an evitable consideration and highly appraised. Dopa/catechol-functionalized PEG's form hydrogels upon their treatment with oxidizing agents such as sodium periodate; the hydrogel is the result of the *o*-quinones formation, generating the crosslinking therefrom. Although the robustness of hydrogel is usually sought for, Dopa groups in the formed hydrogels prove to be the key for setting the required mechanical moduli for biomedical uses; that is, storage modulus *G'* of the order of 10 kPa and loss modulus *G"* of within 1 kPa. Some of these hydrogels are promising tissue sealants such as a fetal membrane sealant for iatrogenic preterm premature rupture of membranes (Haller et al., 2011; Brubaker & Messershmith, 2011). The injectable hydrogel engineered by crosslinking the polymer made by polycondensation of citric acid, PEG, and Dopa with sodium periodate in PBS buffer solution, is characterized by a suture propensity, a prompt healing of created incision (Mehdizadeh et al., 2012; Wilker, 2014). Another injectable hydrogel for healing the human tissue consists of catechol-conjugated chitosan and thiol-terminated Pluronic (Pluronic: copolymer composed of poly(ethylene oxide)-poly(propylene oxide)-poly(ethylene oxide)) (Ryu et al., 2011).The hydrogel based on dopamine-functionalized alginate showed a capacity of healing the arterial incisions, and a drug-eluting for blood vessels and atherosclerotic plaques (Kastrup et al., 2012).

Dopa-grafted copolymers of butadiene and maleic anhydride were designed for itraconozale delivery (Schestopol et al., 2005). Catechol-tethered PEG stands as a cancer drug releasing propensity. Indeed, Bortezomib, a cancer drug, can be carried by this material and be delivered to enhance cytotoxicity against breast cancer cells (Su et al., 2011). Doxorubicin, another effective cancer drug, can be loaded in core-crosslinked micelles formed by dopamine-grafted triblock copolymer (monomethoxypoly(ethylene glycol)-*b*-poly(2-methyl-2-carboxyl-propylene carbonate)-*b*-poly(*L*-lactide)) (Wu et al., 2012). Polydopamine-coated substrates and catechol-modified ones could serve as carriers or immobilizers of biomolecules such as trypsin, heparin, bovine serum albumin (BSA), proteins, and DNA. The immobilization of polylysine on polydopamine-coated substrates helps culturing neurons that show good growth and formation of neuronal networks (Kang et al., 2011). Molecules bearing alkyl quaternary ammonium that can ensure an antimicorbial activity or a corrosion inhibition could be embedded as a co-monomer in copolymers of dopamine-based monomers such as dopamine methacrylamide; obviously, the latter secures the coating on substrate.

Adhesive property of the mussel catechol-grafted polymers has been valorized in nanoscience includingoptics, electronics, photonics, and medicine. Assembling nanoparticles (gold, silver, iron oxide, quantum dots) through catechol units can be accomplished by using catechol-modified polymers such as cotton and hyaluronic acid (Lee et al., 2010;

Xu et al., 2011). The fact that the inhibitionof *Escherichia coli* is almost complete and its reduced rate using the polydopamine-cotton/Ag nanoparticles would hint at the potency of mussel-adhesive property of polydopamine. Peptide/hydroxyapatite nanocomposites, bone-like materials, can be assembled by coating them with polydopamine (Ryu et al. 2011). Electrodes of silicon nanoparticles bound with dopamine-grafted poly(acrylic acid) and dopamine-grafted alginate showed good galvanostatic properties (Ryou et al., 2013). It is possible to coat the nanotube-Ru(bpy)$_3^{2+}$, an electrochemiluminescent sensor immobilized on glassy carbon electrode, with polydopamine to end up with hydrophilic sensing electrode (Xing & Yin, 2009)Uptake and release of dyes such as rhodamine 6G can be achieved using polydopamine nanocapsules (Yu et al., 2009). Encapsulation of gold and silver nanoparticles in Dopa-functionalized polymers shells is believed to occur via the reduction of the metal ions (Au^{3+}, Ag^{+}) by the redox property of catechol units of the Dopa groups (Black et al., 2011).

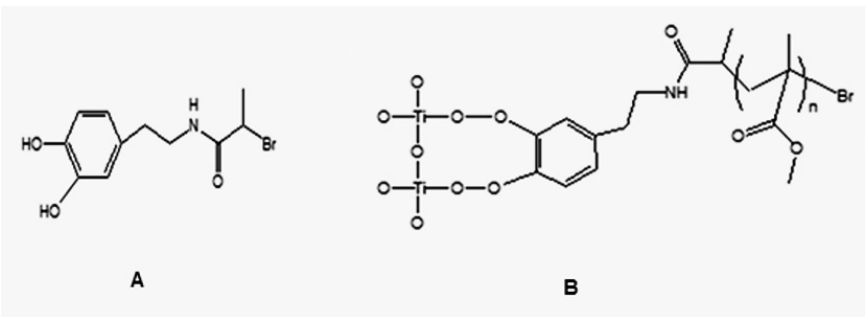

Fig. 11. **A**: ATRP catechol-bearing initiator; **B**: Poly(methyl methacrylate)-grafted TiO_2 nanoparticle

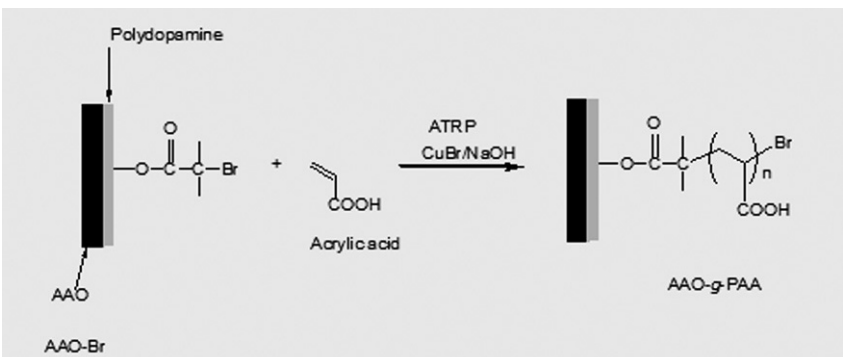

Fig. 12. Polymerization of acrylic acid by SI-ATRP technique

As far as polymer synthesis is concerned, research has been pointed to the use of *Mfp*-inspired materials in surface-initiated polymerization (SIP). First, the polymerization initiating species is chemically attached to catechol-containing molecule, and the thus-obtained system is anchored to a surface through the catechol functionality, and the initiation may start in the presence of a suitable monomer. Few examples are herein cited. SI-ATRP technique (SIP method coupled with atom transfer radical polymerization) was applied to the polymerization of methyl methacrylate (MMA) (Fan et al., 2006); to this end, the ATRP initiator was conceived as the one shown in Fig.11**A** and immobilized on TiO_2 nanoparticles. Poly(methyl methacrylate)-grafted TiO_2 nanoparticle (Fig. 11**B**), a polymer functionalized metal oxide nanoparticle, was obtained. PMMA could be subsequently exfoliated from the metal oxide nanoparticle as desired. On the other hand, PMMA brushes were skillfully designed and elegantly made via the SI-ATRP method on macroscopic planar substrates and nanoscaled ones such as graphene oxide and carbon nanotubes, using a catechol-containing macro-initiator (Wei et al., 2012).

Another strategy is to apply catechol-bearing film on a surface and affix the initiating species. For example, anodic aluminum oxide membrane (AAO) as surface was first coated with polydopamine film, then, this film reacts with 2-bromoisobutyryl bromide, the initiator precursor for the SI-ATRP polymerization of acrylic acid as pictured in Fig. 12 (Wang et al., 2010).

NOTES

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REFERENCES

Bandara, N., Zeng, H. & Wu, J. (2013). Marine mussel adhesion: biochemistry, mechanisms, and biomimetics, *J. Adhes. Sci.& Technol.*, *27*, 2139-2162..

Black, K.C.L., Liu, Z. & Messersmith, P.B. (2011). Catechol redox induced formation of metal core-polymer shell nanoparticles. *Chem. Mater.*, *23*, 1130-1135.

Bouten, P.J.M., Zonjee, M., Bender, J., Yauw, S.T.K., von Goor, H., & van Hest, J.C.M. (2014). The chemistry of tissue adhesive materials. *Prog. Polym. Sci., 39*, 1375-1405.

Brubaker, C.E.& Messersmith, P.B. (2011). Enzymatically degradable mussel-inspired adhesive hydrogel. *Biomacromolecules*, *12*, 4326-4334.

Dalsin, J.L. & Messersmith, P.B. (2005). Bioinspired antifouling polymers. *Mater. Today*, *8*, 38-46.

Fan, X., Lin, L. & Messersmith, P.B. (2006). Surface-initiated polymerization from TiO_2 nanoparticle surfaces through a biomimetic initiator: A new route toward polymer-matrix nanocomposites. *Compos. Sci. Technol.*, *66,* 1195-1201.

Favi, P.M., Yi, S., Lenaghan, S.C., Xia, L. & Zhang, M. (2014). Inspiration from the nat-

ural world: from bio-adhesives to bio-inspired adhesives. *J. Adhes. Sci. & Technol., 28*, 290-319.

Haller, C.M., Buerzle, W., Brubaker, C.E., Messersmith, P.B., Mazza, E., Ochsenbein-Koelble, N., Zimmermann, R. & Ehrbar, M. (2011). Mussel-mimetic tissue adhesive for fetal membrane repair: A standardized *ex vivo* evaluation using elastomeric membranes. *Prenat. Diagn.*, *31*, 654-660.

Hinman, M.B., Jones, J. A., Lewis & R. V. (2000), Synthetic spider silk: a modular fiber. *Trends in Biotechnology*, 18, 374-379.

Holten-Andersen, N., Harrington, M.J., Birkedal, H., Lee, B.P., Messersmith, P.B., Lee, K.Y.C. & Waite, J.H. (2011). pH-Induced metal ligand cross-links inspired by mussel yield self-healing polymer networks with near-covalent elastic moduli. *Proc. Natl. Acad. Sci. USA*, *108*, 2651-2655.

Jacob, J.-L., d'Auzac, J. & Prevôt, J.-C. (1993). The composition of natural latex from *Hevea Brasiliensis. Clin. Rev. Allerg*., *11*, 325-337.

Jenkins, C.L., Meredith, H.J. & Wilker, J.J. (2013). Molecular weight effects upon the adhesive bonding of a mussel mimetic polymer. *ACS Appl. Mater. Interfaces*, *5*, 5091-5096.

Kaneko, D., Wang, S., Matsumoto, K., Kinugawa, S., Yasaki, K., Chi, D.H. & Kaneko, T. (2011). Mussel-mimetic strong adhesive resin from bio-based polycoumarates. *Polym. J, 43*, 855-858.

Kang, K., Choi, I.S. & Nam, Y. (2011). A biofunctionalization scheme for neural interfaces using polydopamine polymer. *Biomaterials*, *32*, 6374-6380.

Kastrup, C.J., Nahrendorf, M., Figueiredo, J.L., Lee, H., Kambhampati, S., Lee, T., Cho, S.-W., Gorbatov, R., Iwamoto, Y., Dang, T.T., Dutta, P., Yeon, J.H., Cheng, H., Pritchard, C.D., Vegas, A.J., Siegel, C.D., MacDougall, S., Okonkwo, M., Thai, A., Stone, J.R., Coury, A.J., Weissleder, R., Langer, R. & Anderson, D.G. (2012). Painting blood vessels and atherosclerotic plaques with an adhesive drug depot. *Proc. Natl. Acad. Sci. USA*, *109*, 21444-21449.

Ku, S. H., Ryu, J., Hong, S. K., Lee, H. & Park, C.B. (2010). General functionalization route for cell adhesion on non-wetting surfaces. *Biomaterials*, *31*, 2535-2541.

Lee, B.P., Chao, C.-Y., Nunalee, F.N., Motan, E., Shull, K.R. & Messersmith, P.B. (2006a). Rapid gel formation and adhesion in photocurable and biodegradable block copolymers with high DOPA content. *Macromolecules*, *39*, 1740-1748.

Lee, H., Scherer, N.F. & Messersmith, P.B. (2006b). Single-molecule mechanics of mussel adhesion. *Proc. Natl. Acad. Sci. USA*, *103*, 12999-13003.

Lee, H., Lee, Y., Statz, A.R., Rho, J., Park, T.G. & Messersmith,P.B. (2008). Substrate-independent layer-by-layer assembly by usingmussel-adhesive-inspired polymers. *Adv. Mater.*, *20*, 1619-1623.

Lee, Y., Lee, H., Messersmith, P.B. & Park,T.G. (2010). A bioinspired polymeric template

for 1D assembly of metallic nanoparticles, semiconductor quantum dots, and magnetic nanoparticles.*Macromol. Rapid Commun.*, *31*, 2109-2114.

Lin, Q., Gourdon, D., Sun, C., Holten-Andersen, N., Anderson, T.H., Waite, J.H. & Israelachvili, J.N. (2007). Adhesion mechanisms of the mussel foot proteins mfp-1 and mfp-3. *Proc. Natl. Acad. Sci. USA*, *104*, 3782-3786.

Liu, Y. & Li, K. (2006).Preparation and characterization of demethylated lignin-polyethylenimine adhesives. *J. Adhes.*, *82*, 593-605.

Matos-Pérez, C.R. & Wilker, J.J. (2012) Ambivalent adhesives: Combining biomimetic cross-linking with antiadhesiveoligo(ethylene glycol). *Macromolecules*, *45*, 6634-6639.

Matos-Pérez, C.R., White, J.D. & Wilker, J.J. (2012). Polymer composition and substrate influences on the adhesive bonding of a biomimetic, cross-linking polymer. *J. Am. Chem. Soc.*, *134*, 9498-9505.

Mehdizadeh, M. & Yang, J. (2013). Design strategies and applications of tissue bioadhesives. *Macromol. Bioscience,13*, 271-288.

Mehdizadeh, M., Weng, H., Gyawali, D., Tang, L. & Yang,J. (2012). Injectable citrate-based mussel-inspired tissue bioadhesives with high wet strength for sutureless wound closure. *Biomaterials*, *33*, 7972-7983.

Meredith, H.J., Jenkins, C.L. & Wilker, J.J. (2014). Enhancing the adhesion of a biomimetic polymer yields performance rivaling commercial glues. *Adv. Funct. Mater., 24,* 3259-3267.

Messersmith, P.B., Lee, H., Lee, Y., Liu, Z. & Hamming, L. (2012). Substrate-independent layer-by-layer assembly by using catechol-functionalized polymers. *US Patent* 8, 293, 867, B2, Oct. 23.

Moulay, S. (2007). In organic chemistry synthesis, never give up, keep trying! *L'Actualité Chim*., *311*, 11-20.

Moulay, S. (2014). Dopa/catechol-tethered polymers: Bioadhesives and biomimetic adhesive materials. *Polym. Rev.*, *54*, 436-513.

Neto, A.I., Meredith, H.J., Jenkins, C.L. , Wilker, J.J. & Mano, J.F. (2013). Combining biomimetic principles from the lotus leaf and mussel adhesive: Polystyrene films with superhydrophobic and adhesive layers. *RSC Adv*., *3*, 9352-9356.

Neto, A.I., Cibrão, A.C., Correia, C.R., Carvalho, R.R., Luz, G.M., Ferrer, G.G., Botelho, G., Picart, C., Alves, N.M. & Mano, J.F. (2014). Nanostructured polymeric coatings based on chitosan and dopamine-modified hyaluronic acid for biomedical applications. *Small*, *10*, 2459-2469.

Nicolaou, K.C., Vourloumis, D., Winssinger, N. & Baran, P.S. (2000). The art and science of total synthesis at the dawn of the twenty-first century. *Angew. Chem. Int. Ed.,* 39, 44-122.

Petrone, L. (2013). Molecular surface chemistry in marine bioadhesion. *Adv. Colloid & Interface Sci.*, *195-196*, 1-18.

Ryou, M.-H., Kim, J., Lee, I., Kim, S., Jeong, Y.K., Hong, S., Ryu, J.H., Kim, T.-S., Park, J.-K., Lee, H. & Choi, J.W. (2013). Mussel-inspired adhesive binders for high-performance silicon nanoparticle anodes in lithium-ion batteries. *Adv. Mater.*, *25*, 1571-1576.

Ryu, J., Ku, S.H., Lee, M. & Park, C.B. (2011). Bone-like peptide/hydroxyapatite nanocomposites assembled with multi-level hierarchical structures. *Soft Matter*, *7*, 7201-7206.

Ryu, J.H., Lee, Y., Kong, W.H., Kim, T.G., Park, T.G. & Lee, H. (2011). Catechol-functionalized chitosan/Pluronic hydrogels for tissue adhesives and hemostatic materials. *Biomacromolecules*, *12*, 2653-2659.

Rzepecki, L.M. & Waite, J.H. (1991). Quinone chemistry: applications in bioadhesion (pp. 229-243). In: Gebelein, C.G. (Ed). *Biotechnology and polymers*. New York: Plenum Press.

Sahni, V., Blackledge, T. A. & Dhinojwala, A. (2011). A review on spider silk adhesion. *J. Adhes.*, *87*, 595-614.

Schestopol, M., Jacob,J., Donnelly, R., Ricketts, Th., Nangia, A., Mathiowitz, E. & Shaked,Z. (2005). Bioadhesive polymers with catechol functionality, *US Patent*, 2005/0201974 A1, Sept. 15.

Statz, A.R., Meagher, R.J., Barron, A.E. & Messersmith, P.B. (2005). New peptidomimetic polymers for antifouling surfaces. *J. Am. Chem. Soc.*, *127*, 7972-7973.

Statz, A., Finlay, J., Dalsin, J., Callow, M., Callow, J.A. & Messersmith, P.B. (2006). Algal antifouling and fouling-release properties of metal surfaces coated with a polymer inspired by marine mussels. *Biofouling*, *22*, 391- 399.

Su, J., Chen, F., Cryns, V.L. & Messersmith,P.B. (2011). Catechol polymers for pH-responsive, targeted drug deliveryto cancer cells. *J. Am. Chem. Soc.*, *133*, 11850-11853.

Thiel, R.J. (2000). Natural vitamins may be superior to synthetic ones. *Med. Hypotheses*, *55*, 461-469.

Vollrath, F. (2000). Strength and structure of spiders' silks. *Rev. Mol. Biotechn.*, *74*, 67-83.

Vollrath, F., Porter, D., & Holland, C. (2011). There are more lessons still to be learned from spider silks. *Soft Matter*, *7*, 9595-9600.

Von Byern, J. & Grunwald, I. (2010). *Biological adhesive systems, from nature to technical and medical application*. Wien: Springer.

Waite, J.H. (1999). Reverse engineering of bioadhesion in marine mussels. *Ann. N. Y. Acad. Sci.*, *875*, 301-309.

Waite, J.H. (2002). Adhesion à la moule. *Integr. Comp. Biol.*, *42*, 1172-1180.

Waite, J.H. & Tanzer, M.L. (1981). Polyphenolic substance of *Mytilusedulis*: Novel adhesive containing *L*-dopa and hydroxyproline. *Science*, *212*, 1038-1040.

Wang, W.-C., Wang, J., Liao, Y., Zhang, L., Cao, B., Song, G. & She, X. (2010). Surface initiated ATRP of acrylic acid on dopamine-functionalized AAO membranes. *J. Appl. Polym. Sci.*, *117*, 534-541.

Wei, Q., Wang, X. & Zhou, F. (2012). A versatile macro-initiator with dual functional anchoring groups forsurface-initiated atom transfer radical polymerization on various substrates. *Polym. Chem.*, *3*, 2129-2137.

Westwood, G., Horton, T.N. & Wilker, J.J. (2007). Simplified polymer mimics of cross-linking adhesive proteins. *Macromolecules*, *40,* 3960-3964.

Wilker, J.J. (2014), Self-healing polymers: sticky when wet. *Nature Materials*, *13*, 849-850.

Wu, S., Kuang, H., Meng, F., Wu, Y., Li, X., Jing, X. & Huang,Y. (2012). Facile preparation of core cross-linked micelles from catechol-containing amphiphilic triblock copolymer. *J. Mater. Chem.*, *22*, 15348-15356.

Xi, Z.-Y., Xu, Y.-Y., Zhu, L.-P., Wang, Y. & Zhu, B.-K. (2009). A facile method of surface modification for hydrophobic polymer membranesbased on the adhesive behavior of poly(DOPA) and poly(dopamine). *J. Membr. Sci.*, *327*, 244-253.

Xing, B. & Yin, X.-B. (2009). Novel polydopamine adhesive for a halloysite nanotube-Ru(bpy)$_3^{2+}$electrochemiluminescent sensor. *PLoS ONE*, *4*, e6451 (1-8).

Xu, H., Shi, X., Ma, H., Lv, Y., Zhang, L. & Mao, Z. (2011). The preparation and antibacterial effects of Dopa-cotton/AgNPs. *Appl. Surf. Sci.*, *257*, 6799-6803.

Yang, W. J., Neoh, K.-G., Kang, E.-T., Teo, S. L.-M. & Rittscho, D. (2014). Polymer brush coatings for combating marine biofouling. *Prog. Polym. Sci.,39*, 1017-1042.

Yu, B., Wang, D.A., Ye, Q., Zhou, F. & Liu, W. (2009). Robust polydopamine nano/microcapsules and their loading and release behavior. *Chem. Commun.*, 6789-6791.

Yu, F., Chen, S., Chen, Y., Li, H., Yang, L., Chen, Y. & Yin, Y. (2010). Experimental and theoretical analysis of polymerization reaction process on the polydopamine membranes and its corrosion protection propertiesfor 304 stainless steel. *J. Mol. Struct.*, *982*, 152-161.

Zeng, H., Hwang, D.S., Israelachvili, J.N. & Waite,J.H. (2010). Strong reversible Fe^{3+}-mediated bridging between Dopa-containing protein films in water. *Proc. Natl. Acad. Sci. USA*, *107*, 2850-12853.

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