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Opinion

# Toxic Building Blocks Can Yield Highly Biocompatible Materials: New Perspectives for Biomaterials Science

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## Opinion

A material can only be considered as a biomaterial when it does not result in a negative response (excessive inflammatory response, excessive foreign body response, etc.) by the organism in which it is implanted or put in contact. This implies that a biomaterial has to be biocompatible, non-cytotoxic and to have mechanical properties allowing its interaction, including adhesion, with the vicinal cells and tissues. Even if biomaterials science has undergone major developments in the last years to use not only passive materials but also active materials (undergoing controlled degradation and recolonization by the cells of the host) and even so called living biomaterials [1], we have to admit that the range of materials used is pretty limited in comparison with the large repertoire used in other fields of materials science. Indeed, it is restricted to a set of metals (with controlled mechanical properties and modified or alloyed to reduce their corrosion), to different ceramics and to polymers like hydrolysable esters [poly (-L-Lactic acid), poly (ε-caprolactone), etc] and polymers inspired from the extracellular matrix, namely polysaccharides. The research in the field is often limited by this relatively restricted range of available materials to be tested as potential biomaterials. To enlarge the possibilities and properties of biomaterials, an emerging field consists in the design of combinatorial biomaterials [2]. Nevertheless, in such experiments use is made of a rather limited set of chemical moieties, often neglecting the use of molecules which are considered and recognized as toxic. The aim of this opinion is to point to the fact that a priori extremely toxic molecules can undergo chemical pathways leading to highly biocompatible materials. Two prototypal examples appeared in the recent literature, namely materials derived from dopamine and aminomalononitrile para-toluene sulfonate (Figure 1).

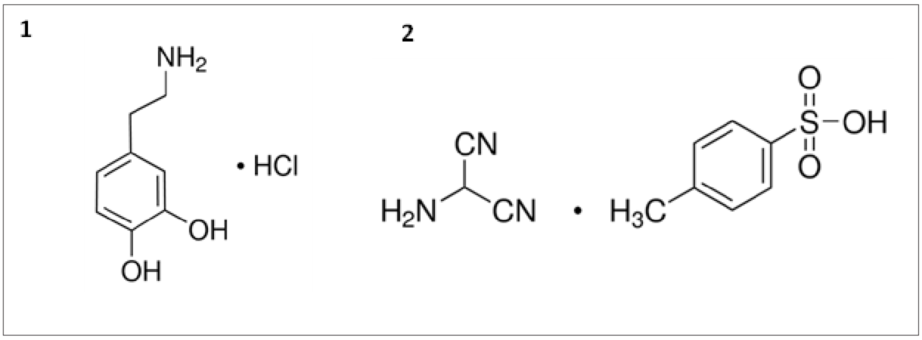


**Figure 1:** Structure of dopamine hydrochloride (1) and aminomalononitrile para-toluene sulfonate (2) as toxic compounds allowing to produce highly compatible biomaterials under controlled reaction conditions.

Dopamine, a neuro mediator, is not able to cross the blood–brain barrier in normal conditions but when injected in the blood circulation it can cause tachycardia. Aminomolonitrile, the trimer of HCN, on the other hand can undergo partial hydrolysis to produce the highly toxic hydrogen cyanide.

But in the presence of an oxidant dopamine yields to a material, called polydopamine, which forms a conformal film on the surface of all materials [3]. This film is easy to post-functionalize owing to the simultaneous presence of catechol (allowing for metal coordination and reduction) and quinone moieties (allowing for nucleophilic attack). In addition, polydopamine films are highly biocompatible displaying common features with the eumelanin of the skin [4]. Concerning aminomalononitrile, when put in an alkaline aqueous solution, it undergoes a complex chemical pathway leading to peptides in solution [5] and to the deposition of a conformal [6] and nanostructured coating [7] adhering again on the surface of almost all known materials [6]. In addition, these coatings are highly biocompatible for fibroblasts and other cell lines [6]. They are in addition favorable for bone-integration [8] and can be made antifouling when blended with appropriate polymers [9]. These two particular examples of toxic compounds leading to highly biocompatible films and coatings or hydrogels may be taken as prototypal in the design of new potential biomaterials. Finally, the absence of cytotoxicity comes only into consideration for the final material and its degradation product which may not be identical than the initially used toxic reagents. This may open our mind for the design of new biomaterials.

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