Safe(r) By Design alternatives of nanosilver-enabled wound dressings

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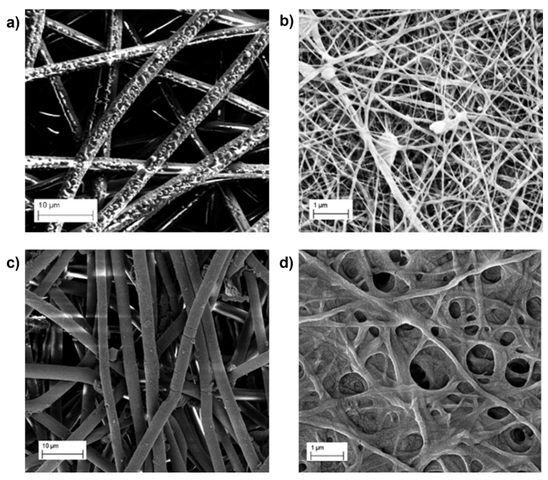
Objectives and methods

The use of silver nanoparticles (NPs) in medical devices is constantly increasing due to their excellent antimicrobial properties. In wound dressings, Ag NPs are commonly added in large excess to exert a long-term and constant antimicrobial effect, provoking an instantaneous release of Ag ions during their use or the persistence of unused NPs in the wound dressing that can cause a release of Ag during the end-of-life of the product. For this reason, the main actions of this work were to:

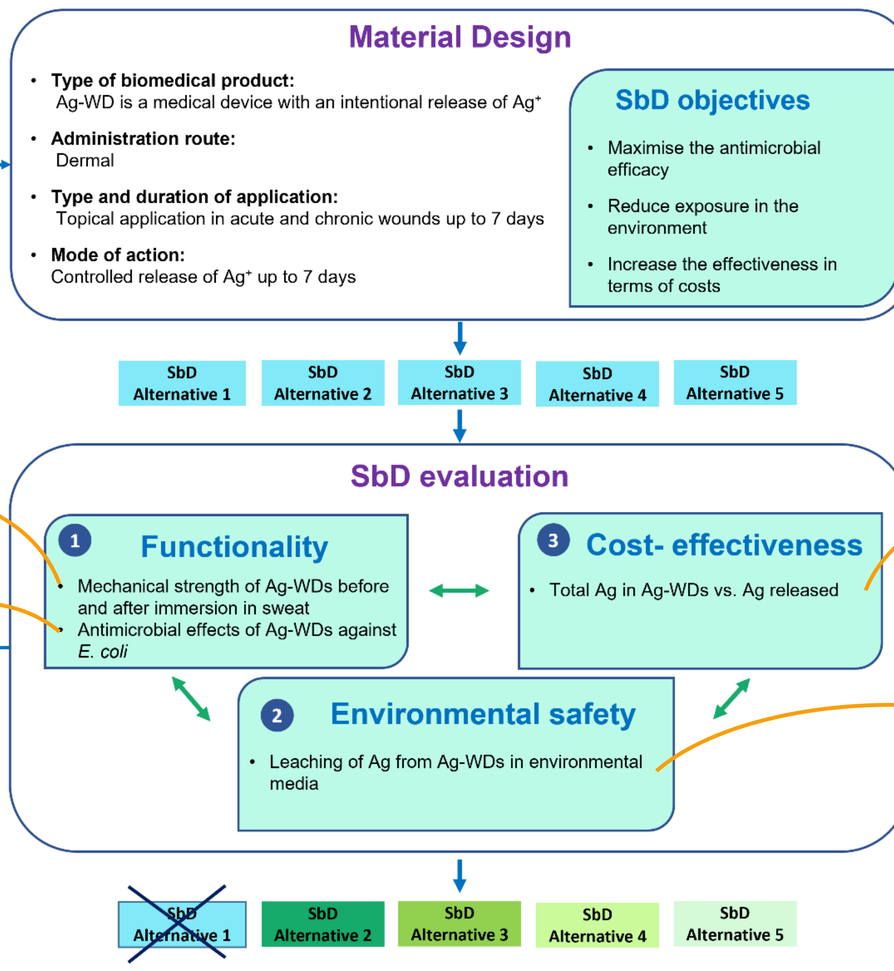
1. Develop a **SbD procedure for nanosilver enabled-wound dressings** (Ag-WDs) considering the selected SbD objectives and using environmental/human health criteria based on previous SbD papers.
2. Perform **ad-hoc experimental tests** (e.g., antimicrobial tests of the Ag-WDs, leaching of Ag from the Ag-WDs) specific for each criterion assessing functionality, environmental safety and cost- effectiveness of the Ag-WDs.
3. Identify **the safer alternative among five Ag-WDs** which differ among the type, the quantity of Ag NPs and the type of polymer used in the matrix, and compare results with two commercial Ag-WDs.

Results: SbD procedure and its application



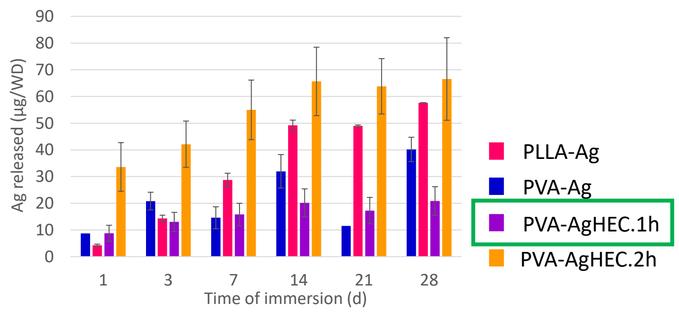
SEM images before immersion of a) PLLA-Ag, b) PLLA-AgHEC, and after 24h of immersion in synthetic sweat of c) PLLA-Ag and d) PLLA-AgHEC. Because of its low mechanical strength after immersion, PLLA-AgHEC was not considered in further analysis.

Ag-WDs	Bacterial reduction % (*E. coli*)
PVA-Ag	89
PLLA-Ag	97
PVA-AgHEC.1h	100
PVA-AgHEC.2h	100
Acticoat Flex 3	-
Acticoat Flex 7	-



$$\text{Cost-Effectiveness (CE) \%} = \frac{Total\ Ag}{Ag\ released_{sweat}} \text{ X } 100$$

Ag-WDs	CE (%) at day 1	CE (%) at day 3	CE (%) at day 7
PVA-Ag	6.9	12.7	24.2
PLLA-Ag	0.1	0.2	0.4
PVA-AgHEC.1h	26.4	33.8	49.0
PVA-AgHEC.2h	26.9	31.1	45.0
Acticoat Flex 3	0.2	0.2	0.3
Acticoat Flex 7	0.2	0.2	0.2



Leaching of silver from Ag-WDs immersed in Artificial Marine Water

Final evaluation and conclusions

- The SbD procedure permits to **select the best alternative** among five different SbD nanosilver-enabled wound dressings
- Additional **human health and environmental criteria** (e.g., (eco)tox data) can be included in future SbD approaches
- This work highlights the **importance to reduce Ag content** (added in large excess in commercial Ag-WDs) **while maintaining an effective antimicrobial efficacy**

Wound Dressing	SbD criteria				
	Functionality - antimicrobial activity -	Environmental safety - leaching tests			Cost-effectiveness
		in AFW	in AMW	in S:W extract	
PVA-Ag					
PLLA-Ag					
PVA-AgHEC.1h					
PVA-AgHEC.2h					

Best alternative → Worst alternative

Further information can be found in the article: Cazzagon V., Giubilato E., Bonetto A., Blosi M., Zanoni I., Costa A. L., Vineis C., Varesano A., Marcomini A., Hristozov D., Semenzin E. *, Badetti E.* (in press). *Identification of the Safe(r) By Design alternatives of nanosilver-enabled wound dressings*, Frontiers in Bioengineering and Biotechnology, Section Nabiotechnology.

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