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## <u>Multitarget drugs in cardiovascular diseases: New agents with antioxidant and vasodilating properties for chronic applications</u>

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ardiovascular diseases (CVDs) comprise a group of diseases and disorders of the heart and blood vessels, which together are the number one cause of death worldwide. For a long time, the search for \_ was based on the old paradigm "one compound - one target", aiming to obtain a highly potent and selective molecule with only one desired molecular target. This approach ignores the multiple causes and the multifactorial nature of CVDs. Thus, over time, treatment strategies for cardiovascular diseases have changed, and, currently, pharmacological therapies for CVD are mainly based on the association of two or more drugs. In this context, the multitarget approach can overcome some limitations of classic therapy. Multitargeting drugs are the result of the conjugation of two or more single target inhibitors, they are compounds having the ability to act simultaneously at multiple sites. This is an attractive and relevant strategy that can have the advantage to achieve easier predictable pharmacokinetic and pharmacodynamics profiles as well as be In this occasion new phenols-organic nitrate are presented as tter patient compliance. Vasodilating agents endowed of antioxidant properties with the aim to overcome tolerance problems. Oxidative stress has been in fact identified as one of responsible of tolerance development; the hypothesis is that the ROS are involved in the inactivation of ALDH-2, the enzyme associated with bioactivation of nitrates leading to Nitric Oxide release. This study suggests a potential role for multitarget drugs antioxidant NO-donor organic nitrates, as a therapeutic tool in the prevention or control of the tolerance that accompanies the chronic use of <u>organic nitrates</u> in patients.

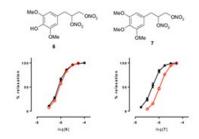


Figure 1: Structures of compounds 6 and 7 and Concentrationresponse curves in control experiments (black ●) and tolerant vessels (red o) of compound 6 and compound 7

## **Biography**

Marta Giorgis is a member of the Medicinal Chemistry team of the DSTF since 2008, she is an expert in biological tests; over the years she has gained her experience studiing antioxidant properties of compounds and working with inhibitors of various human and animal enzymes. Moreover she became expert in the determination of the in vitro ADME profile of new chemical entities, fundamental step of the Hit to lead process.

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