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STATUS OF GLUTATHIONE AND OTHER THIOLS IN HUMAN PLASMA DURING AGING

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GSH, the most important cellular thiol for abundance of enzymes and concentration, is expressed at negligible levels in plasma (below 10 μM). By contrast other thiols, such as cysteine, cysteinilglycine and homocysteine, are relatively low intracellularly (their total sum is less than 0.2-0.4 mM with respect to GSH that ranges between 2-6 mM), whereas they have the same or higher concentration than GSH in plasma. Conversely, the intracellular compartment, plasma is characterized by high levels of oxidized thiols, being for example, cystine 4-8 fold higher than cysteine. The biological reason of the characteristic distribution of plasma thiols (and corresponding disulfides and protein mixed disulfides) is unknown.
In a previous clinical study on the plasma distribution of thiols in subjects with cardiovascular diseases we found that the cysteine pattern was correlated with homocysteine but not with GSH. Cysteine is a non-essential aminoacid that is needed for protein and GSH biosynthesis. Its plasma pool may derive from protein catabolism, GSH hydrolysis via gamma-GT activity or transulfuration reactions that in liver convert homocysteine, deriving from methionine, into cysteine. Although different sources may contribute to generate plasma cysteine, it is generally assumed that GSH and the renal gamma-GT activity play a major role.
In this study we have followed the plasma distribution of various endogeneous thiols (cysteine, homocysteine, GSH and cysteinylglycine) and corresponding disulfides and protein mixed disulfides in healthy subjects of different age (from newborn to adult) in order to confirm whether the previous observed correlation between cysteine and homocysteine is maintained during aging. The interest of this study is also related to the great importance that homocysteine has as a risk factor for cardiovascular diseases and other pathologies of radical origin. Although preliminar our results seem to confirm that GSH and cysteinylglycine levels remain unmodified, whereas cysteine and homocysteine increase parallelly with the age.