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What is the relationship between intracellular and extracellular metabolites? The theory of "metabolic overflow" put into test

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Compared to our knowledge on metabolic pathways and the establishment of tools to manipulate these pathways, we know very little about the mechanisms behind the secretion of metabolic intermediates. Microorganisms secrete a wide range of metabolic intermediates, and many of them are of great industrial interest.

Despite the cellular process of metabolite efflux being ubiquitous to all microbial cells, we still do not know clearly how this process works and how it is regulated. It is believed that small metabolites, mainly those end products of fermentation are excreted through the plasma membrane passively, or they are secreted through specialised mechanisms such as vectorial reaction in response to hypo-osmotic stress, or uniport and synport transport systems. However, all of these mechanisms are based on the concept of "metabolic overflow", which under specific metabolic conditions it is observed a massive excretion of some metabolic intermediates due to their intracellular accumulation. Although this concept seems appropriate to explain the secretion of some intracellular metabolites, it does not apply to many cases studied during continuous culture. Our metabolomics data obtained during different time-series studies of microbial growth under continuous and batch cultures confirm that the concept of "metabolic overflow" cannot be applied to explain the efflux of several intracellular metabolites found in the extracellular medium. Most of our studies indicate that microbial cells very often get rid of some intracellular metabolites in response to an environmental stimulus, even if these metabolites are key intermediates of central carbon metabolism.

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