Investigation into the effects of metabolism on the cytotoxicity of a subset of cosmetically-relevant compounds using an animal-product-free assay.

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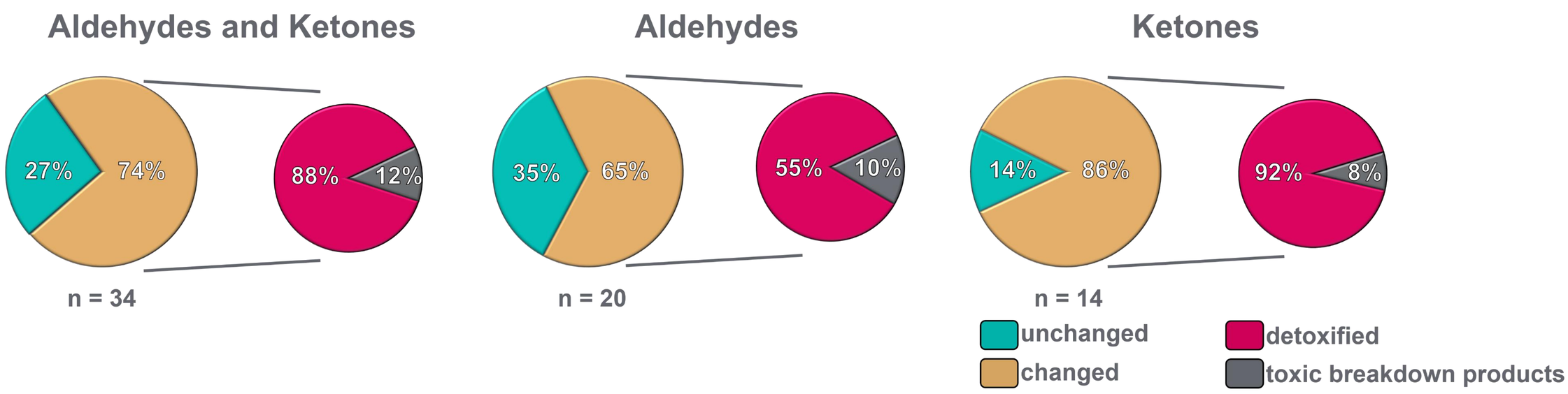
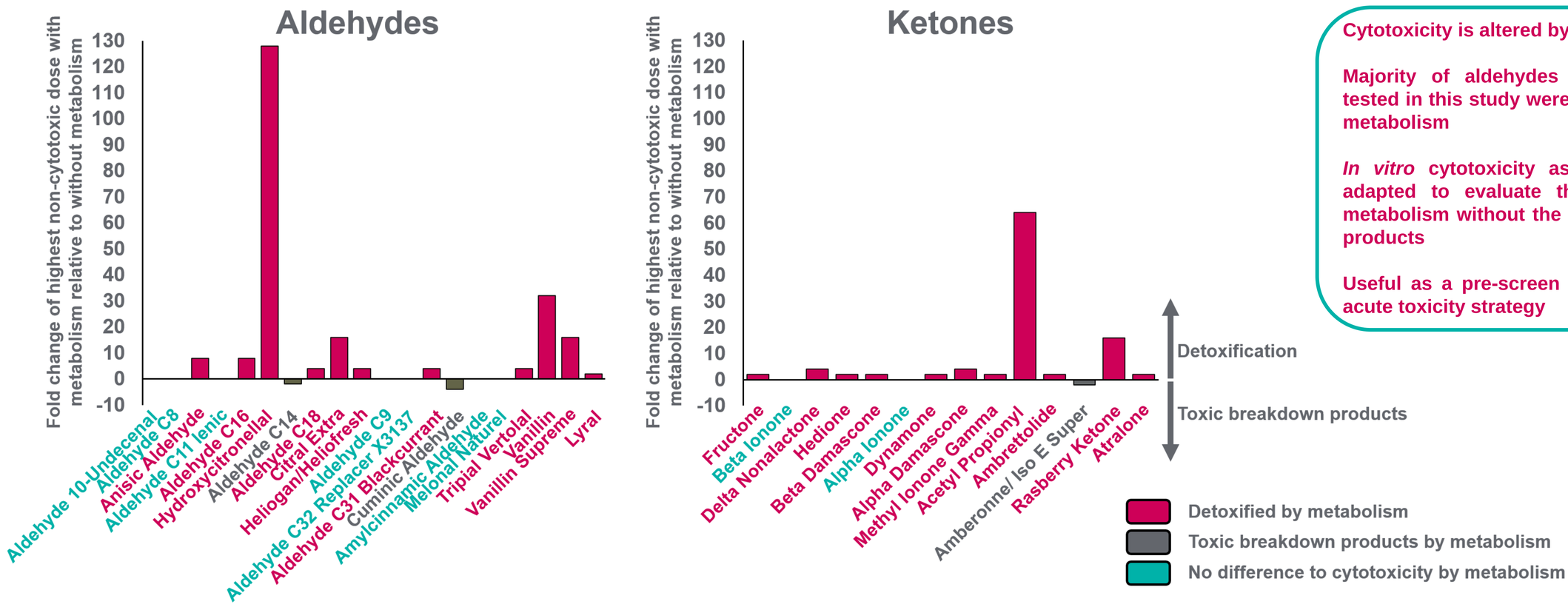
Introduction

The toxicity profiles of a multitude of chemicals are known to change following metabolism in the liver. This is often overlooked in *in vitro* cytotoxicity assays and the effects of metabolic breakdown of compounds (either detoxification or the generation of toxic metabolic by-products) are seldom taken into account in the experimental system. At XCellR8, our laboratory is 100% animal-product free and we have been investigating the effect of metabolism using a Thiazole Orange based cytotoxicity assay. During our investigation we screened compounds that are frequently used as raw ingredients in the cosmetic and fragrance industries and these were categorised based upon their functional groups. The case study presented here will comprise an analysis of cosmetically-relevant, but often cytotoxic, raw ingredients that contain either an aldehyde functional group or the chemically-related ketone moiety.

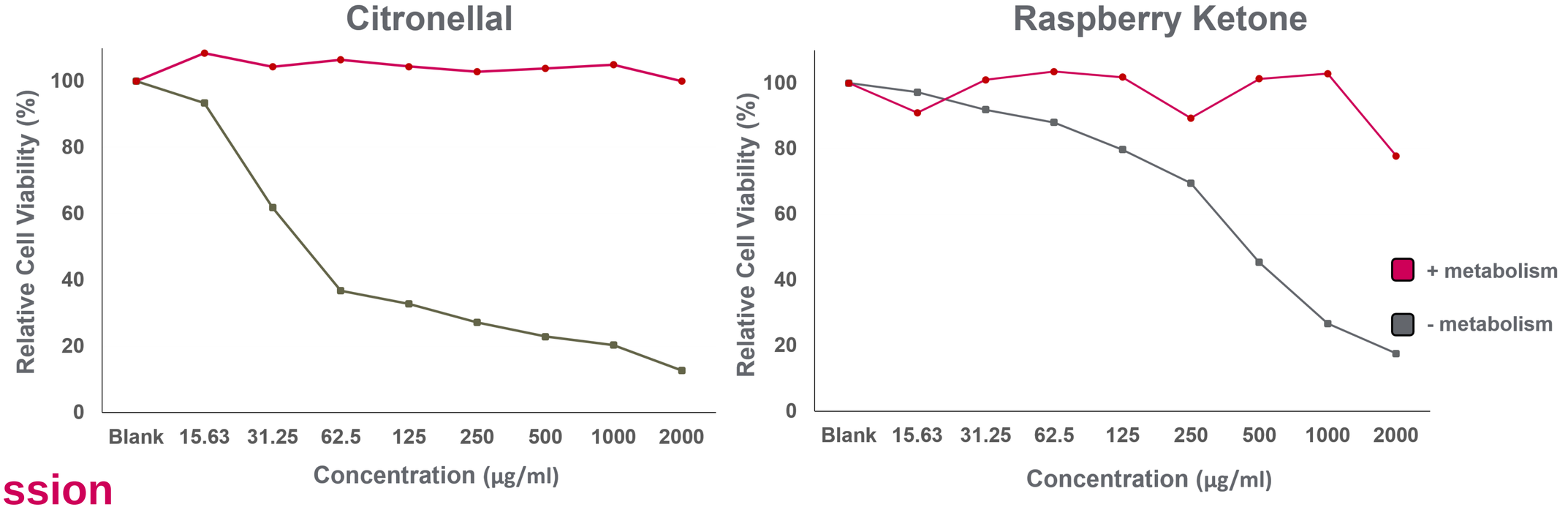
Metabolism alters the cytotoxicity of aldehydes and ketones



Profiling the effects of metabolism using an *in vitro* cytotoxicity screen



Examples: Metabolism detoxifies Citronellal and Raspberry Ketone



Discussion

We demonstrate that the majority (74%) of the toxicity profiles generated for the aldehyde and ketone subgroup is altered by expanding the *in vitro* cytotoxicity test to encompass metabolic functionality. Furthermore, of the toxicity profiles that were altered following exposure to human S9 (facilitates *in vitro* metabolic action), 88% of the results displayed evidence of detoxification, whilst 12% demonstrated the presence of cytotoxic metabolic-breakdown products.

Our results highlight that incorporating metabolic functionality into an animal-product-free *in vitro* cytotoxicity assay provides the basis of a more comprehensive assessment of cytotoxicity that can be performed routinely *in vitro*. This approach yields preliminary raw material screens that are more relevant to human biology and may form part of an *in vitro* strategy for the assessment of human acute toxicity.