Metabolomics reveals metabolic targets and biphasic responses in breast cancer cells treated by curcumin al and in association with docetaxel.

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Several studies have demonstrated that Curcumin exhibits not only anti- but pro-oxidant activities, and that anti-inflammatory and anti-proliferative effects are linked to pro-oxidant activities. Pro-oxidant effect, mostly occuring at high dose, thought to be involving oxidative DNA damage, protein and membrane lipid peroxidation and apoptosis.

Furthermore, many reports have mentioned that antitumor effects of Curcumin are generally underpinned by pro-oxidant effects. Anti- and pro-oxidant effects of Curcumin corroborate well with response to a number of cell stressing agents which is biphasic as a function of dose with a stimulating phase followed by a toxic phase, which is called hormesis, is frequently encountered in the field of nutripharmaceutics.

Different anticancer agents have been evaluated for their mechanism of action using metabolomics, but little has been applied in case of nutritional agents, including Curcumin.

Objective:

To investigate the response of MCF7 and MDA-MB-231 breast cancer cells to increasing doses of Curcumin and that of MCF7 cells to Curcumin in combin with docetaxel (DTX), a therapeutic combination that has been proposed in advanced and metastatic breast cancer using ^{1}H-NMR spectroscopy-b metabolomics.

Study Design:

Study involved human MCF7 and MDA-MB-231 breast carcinoma cells that were evaluated for total DNA content, total glutathione S-transferase (GST) ac and ^{1}H-NMR spectroscopy-based metabolomics.

Results:

Relative DNA content decreased in response to Curcumin

Curcumin demonstrated pro-oxidant effect in MCF7 cells by inducing increased DNA oxidative damage, expressed by tail DNA

Activity of GST was dramatically dropped in cells treated with Curcumin

In case of high and low doses of DTX (i.e. DTX-H and DTX-L), DNA content was decreased at 72 h

A marked increase in relative DNA content was seen when duration of exposure to Curcumin was 24 h with DTX-L and DTX-H

Conclusion:

Overall, it was concluded that ^{1}H-NMR spectroscopy-based metabolomics revealed important targets of Curcumin. Additionally, metabolomics also sh metabolic biphasic responses related to Curcumin that likely accounts for its apparently paradoxical effects used at different doses, in various therap combinations and cell types, including oxidative and inflammatory status.