



Human Intestinal Fungi in Biotransformation of Dihydrocapsaicin

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Abstract

The main bioactive component of Capsicum plants is dihydrocapsaicin, which is used as a food drug and additive in China and India. In this study, four in vitro cultivated human intestinal fungal strains were used to perform the biotransformation of dihydrocapsaicin. Eight metabolites, including seven beforehand undescribed metabolites (1 and 38) and one known simple, were acquired. To determine their structures, numerous spectroscopic data, including NMR and HRESIMS, were collected. The most important biotransformation reactions were identified as hydroxylation, alcohol oxidation, and lactylation based on the structures of the dihydrocapsaicin metabolites. Specifically, the lactylation of hydroxyl bunches is for the most part interceded by *Rhizopus oryzae* R2701.

Keywords: Dihydrocapsaicin, Intestinal fungal strains, Spectroscopic, Biotransformation, Hydroxylation

INTRODUCTION

Capsaicin and dihydrocapsaicin are widely recognized as the primary constituents of Capsicum plants, including hot peppers. Dihydrocapsaicin applies anticancer exercises against different harmful growths, like bosom disease, colorectal malignant growth, and glioma. Capsaicin and its metabolites have recently been found to be effective inhibitors of LSD1. The fact that dihydrocapsaicin derived from a natural product can be utilized in the development of new LSD1 inhibitors has piqued our interest since we discovered that dihydrocapsaicin is also a natural LSD1 inhibitor with an inhibition of 76.5 percent at 10 M in this study. Biotransformation has been widely considered on the grounds that it has been distinguished as a successful strategy for changing over abundant or inexpensive natural mixtures into in any case scant or exorbitant analogs. Due to their similar structures, biotransformation products of the capsaicin side chain appear to have comparable biological activities to capsaicin. Dihydrocapsaicin was biotransformed by human intestinal fungi in order to find more bioactive LSD1 inhibitors. This led to the discovery of eight metabolites, including seven new metabolites and a known analog (Stazi G, 2016). In addition, the inhibitory effect of metabolites on LSD1 was examined. Strikingly, metabolite

1 showed critical inhibitory movement against LSD1, with a restraint pace of 80.7%, which was more grounded than that of dihydrocapsaicin. Besides, metabolite 1 showed most grounded inhibitory impact on LSD1 (IC₅₀ 1.99 μM). In this study, LSD1 was found to be a target of metabolite 1 for the first time. This can serve as a new scaffold for improving the LSD1 inhibitor further. In this, we report subtleties of the biotransformation methodology and theoretical biotransformation pathway of dihydrocapsaicin and the disconnection, structure clarification, and inhibitory impact on LSD1 of the metabolites (Huang Y, 2012) (Lim S et al., 2009).

DISCUSSION

We looked at how dihydrocapsaicin and its metabolites 18 inhibited LSD1. Accordingly, the inhibitory effects of the greater part of the metabolites against LSD1 were viewed as in the scope of 25-60% at 10 μM. Quite, metabolite 1 and dihydrocapsaicin shown huge inhibitory impact on LSD1, with hindrance of 80.7% also, 76.5% at 10 μM, individually (Liang Y, 2009). In addition, the LSD1 inhibitor metabolite 1 had an IC₅₀ value of 1.99 M. Strangely, metabolite 1 showed a higher LSD1 hindrance rate than dihydrocapsaicin, in spite of the fact that they contrasted from one another; just C-9 and C-50 in dihydrocapsaicin were both supplanted by

hydroxyl gatherings (Sakane N et al., 2011) (Musri MM et al., 2010). However, the specific mechanism of this result remains a mystery and requires additional investigation. There have been numerous reports of reversible and irreversible LSD1 inhibitors, but only a few are natural (Janzer A et al., 2012) (Libby P, 2011). For example, baicalin was viewed as the principal LSD1 inhibitor (IC₅₀ 3.01 μM), and α-mangostin was viewed as the first xanthone-based LSD1 inhibitor (IC₅₀ 2.81 μM). Prominently, it has been accounted for capsaicin (IC₅₀ 0.6 μM) and capsaicin simple (9,50-dihydroxycapsaicin) (IC₅₀ 1.52 μM) both showed significant inhibitory impact on LSD1 (Mitra R, 2022) (Wang Yet al., 2009).

CONCLUSION

Dihydrocapsaicin was biotransformed by four intestinal fungi (*Aspergillus japonicus* Y4009A, *Rhizopus oryzae* R2701, *Candida parapsilosis* M8011, and *Aspergillus fumigatus* PB4204) into seven new metabolites and one known analog. The designs were unambiguously resolved utilizing NMR and HRESIMS spectra. The most important biotransformation reactions were identified as hydroxylation, alcohol oxidation, and lactylation based on the structures of the dihydrocapsaicin metabolites. In an in vitro bioassay, metabolite 1 had the greatest inhibitory effect on LSD1 (IC₅₀ of 1.99 M). According to the aforementioned findings, the biotransformation of dihydrocapsaicin by intestinal fungi was an efficient strategy for the production of LSD1 inhibitors that could be utilized as treatments for cancer.

REFERENCES

1. Stazi G, Zwergel C, Valente S (2016). Mai LSD1 inhibitors: a patent review (2010-2015). *Expert Opin Ther Pat.* 26: 565-580.
2. Huang Y, Vasilatos SN, Boric L, Shaw PG, Davidson NE (2012). Inhibitors of histone demethylation and histone deacetylation cooperate in regulating gene expression and inhibiting growth in human breast cancer cells. *Breast Cancer Res Treat.* 131: 777-789.
3. Lim S, Janzer A, Becker A, Zimmer A, Schüle R, et al (2010). Lysine-specific demethylase 1 (LSD1) is highly expressed in ER-negative breast cancers and a biomarker predicting aggressive biology. *Carcinogenesis.* 31: 512-520.
4. Liang Y, Vogel JL, Narayanan A, Peng H, Kristie TM (2009). Inhibition of the histone demethylase LSD1 blocks alpha-herpesvirus lytic replication and reactivation from latency. *Nat Med.* 15: 1312-1317.
5. Sakane N, Kwon HS, Pagans S, Kaehlcke K, Mizusawa Y, et al (2011). Activation of HIV transcription by the viral Tat protein requires a demethylation step mediated by lysine-specific demethylase 1 (LSD1/KDM1). *PLoS Pathog.* 7: e1002184.
6. MM Musri, MC Carmona, FA Hanzu, P Kaliman, R Gomis, et al (2010). Histone demethylase LSD1 regulates adipogenesis. *J Biol Chem.* 285: 30034-30041.
7. Janzer A, Lim S, Fronhoffs F, Niazy N, Buettner R, et al (2012). Lysine-specific demethylase 1 (LSD1) and histone deacetylase 1 (HDAC1) synergistically repress proinflammatory cytokines and classical complement pathway components. *Biochem Biophys Res Commun.* 421: 665-670.
8. Libby P, Ridker PM, GK (2011). Hansson Progress and challenges in translating the biology of atherosclerosis. *Nature.* 473: 317-325.
9. Mitra R, Ayyannan SR (2022). Role of lysine-specific demethylase 1 and its small molecule inhibitors in glioblastoma multiforme therapy, *Anti-Cancer Agents. Med Chem.* 22: 3062-3085.
10. Wang Y, Zhang H, Chen Y, Sun Y, Yang F, et al (2009). LSD1 is a subunit of the NuRD complex and targets the metastasis programs in breast cancer. *Cell.* 138: 660-672.