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Re-examination of 6-Shogaol Biotransformation by *Aspergillus niger*

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We are continuing to examine the biotransformation of pungent vanilloid type plant secondary metabolites obtained from red pepper and ginger by microorganisms and also by mammal enzyme systems. Previously we reported that 6-shogaol (1), a pungent analgesic principle of the rhizome of *Zingiber officinale*, Roscoe (Lee *et al.*, 1986) was transformed by *Aspergillus niger* to produce two main metabolites (Koh and Lee, 1983). The crystalline metabolite obtained after silicic acid column chromatography was proved to be 1-(4'-hydroxy-3'-methoxyphenyl)-decan-10-ol-3-one (2). The oily metabolite obtained after prolonged fermentation was 1-(4'-hydroxy-3'-methoxyphenyl)-decan-3,10-diol (3). We also noticed a novel reductive metabolism of 6-shogaol in rat liver *in vitro* (Surh, 1983, Surh and Lee, 1992, 1994). The α,β-unsaturated keto-system of 6-shogaol was reduced to a saturated ketone (4) and reduced further to a reduced alcohol (5). With these results, we proposed a microbial degradation pathway of shogaol in 1983 (Fig. 1). Recently, two other new metabolites of 6-shogaol were isolated from the fermentation broth of *Aspergillus niger* in addition to the previously known metabolites 2 and 3 (Takahashi *et al.*, 1993). The two newly isolated metabolites were the γ-lactone of 6-(4'-hydroxy-3'-methoxyphenyl)-4-hydroxy-hexanoic acid (6) and homovanillic acid (7). However, Takahash's group could not show a whole sequence of bioconversion pathway of 6-shogaol to the γ-lactone (6). Thus biotransformation of 6-shogaol was re-examined with the previous data obtained from the same species of *Aspergillus*. Many efforts had not been paid to isolate intermediary acidic metabolites of (6)-shogaol from the fermentation broth of *A. niger*. Acidic metabolites like compound 8 and 9 were not accumulated because of their rapid metabolism. Alternatively, capsaicin (10) and its synthetic analog octanoylvanillylamide (11) were chosen. Capsaicin possesses ω-branched acylamide bond and compound 11 possesses the same length of its vanillyl sidechain as 6-shogaol does. When capsaicin was exposed to *A. niger*, as we expected, carboxylic acid form of capsaicin, 2-methyl-N-vanillylcarbamoyl-3-(E)-octanoic acid (12) was accumulated due to its delayed branched acid metabolism. Characterization of this compound was carried out by UV, IR and GC-mass spectroscopic analyses after methylation and also silylation (Lee, 1983). When compound 11 was exposed to the same *A. niger* in a prolonged period of time (10 days), N-vanillylcarbamoyl propionic acid (13), a consecutive β-oxidation product was accumulated. Compound 13 is equivalent to compound 9 which was not accumulated in the fermentation broth. The crystalline compound 13, m.p. 151-152℃, was characterized spectroscopically in the usual manner. On this point one may notice that the amide bond in capsaicinoids definitely blocked further oxidation of the vanillyl side chain. Generally, microorganisms can reduce ketones to secondary alcohols through their dehydrogenase activity. Likewise, keto-acids could be reduced to alcoholic acids and then transformed to lactones. This is evidenced by the fact that exposure of a δ-ketoacid (14) or androst-4-ene-3,17-dione to *Nocardia* gave a δ-lactone (15) (Lee and Sih, 1967). With accumulated evidences through studies on biotransformation of capsaicinoid type vanilloids by *A. niger* and also on a degradation pattern of steroid nucleus by microorganisms, a plausible biotransformation pathway of 6-shogaol to a γ-lactone (6) was herein proposed (Fig. 2).

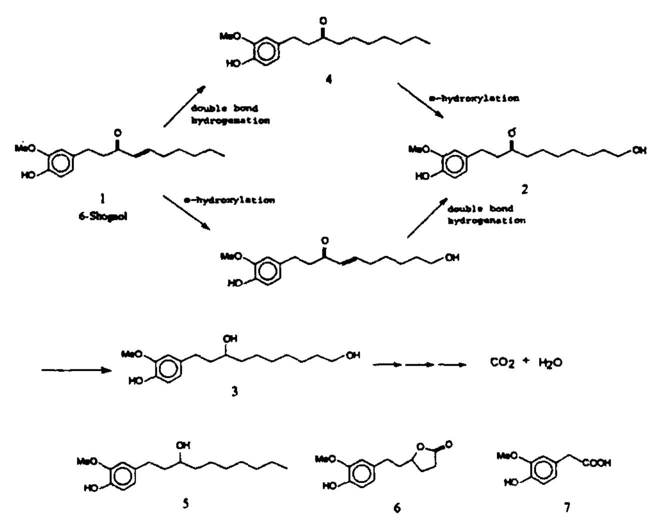

Fig. 1. Biodegradation pathway of (6)-shogaol by *Aspergillus niger*

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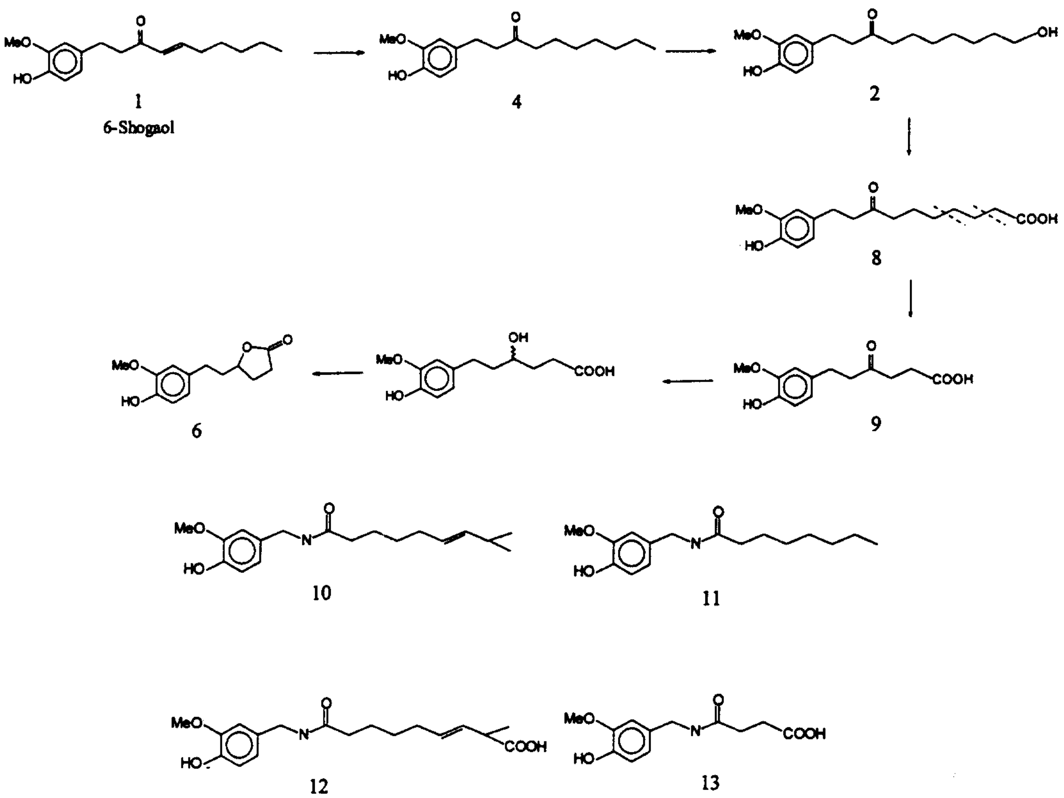

Fig. 2. A biotransformation pathway of 6-shogaol to γ-lactone of 6-(4'-hydroxy-3'-methoxyphenyl)-4-hydroxyhexanoic acid (6).

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