

SUMMARY

Monascus purpureus, used as a food additive, coloring and flavoring agent in foods and beverages in ancient China. Production of secondary metabolites like polyketides, statins, sterol and fatty acids during solid-state and shake flask culture by *M. purpureus* and its mutants through different fermentation conditions were studied. Mutant CFR 410-11 over produced polyketide pigments (1148 OD Units) compared to *M. purpureus* MTCC 410 (604 OD Units). The mutant CFR 410-22 showed low quantity of polyketide pigments (473 OD Units) compared to MTCC 410 in solid-state cultures.

A comparative study made by TLC and HPLC revealed that statin produced by *M. purpureus* and its mutants were similar to the commercial statin with R_f value and retention time. Solid-state cultures produces highest amount of statin compared to shake flask cultures. More sterols are produced in shake flask cultures compared to solid-state. Significant amount of fatty acids production in solid-state than in shake flask cultures were confirmed by GC.

Among the metabolites of *M. purpureus*, lovastatin (Monacolin K) potent inhibitor of 3-hydroxy-3-methylglutaryl-CoA reductase (HMG-CoA) is found to be very important and have been proven to be cholesterol lowering drug. Cultural condition has a significant influence on the yield of statin. Maltose (5.09 mg/g) and peptone (5.53 mg/g) as carbon and nitrogen source with pH 5.0 (5.79 mg/g) and 28° C (5.99 mg/g) is the optimum condition for statin production.

L-asparaginase (0.103 IU) and L-glutaminase (0.139 IU) activity was comparatively more in CFR 410-11 than MTCC 410 and CFR 410-22. The mutant CFR 410-11 secreted more red pigment cultured on rice (2.248 OD Units) and in broth (0.841 OD Units). Significant difference in amidase activities in MTCC 410 and its mutant CFR 410-11 and CFR 410-22 revealed the importance of these enzymes in pigment production.

Safety of RMR was assessed by conducting acute and sub-chronic toxicological studies on both sexes of albino rats. Feeding acute doses of RMR did not cause any symptoms of toxicity or mortality. Similarly, dietary feeding of RMR did not produce any significant changes in food intake or gain in body weight of the experimental rats compared to control rats. No significant differences in the relative weight of vital organs, hematological parameters, macroscopic and microscopic changes in vital organs and serum clinical enzyme levels between the experimental and control groups.

RMR containing lovastatin at a concentration of 11.51g/ kg reduced total cholesterol (TC), triglyceride (TG), lipoprotein cholesterol (LDL) in high fat diet (HFD) fed Wistar rats. There was no significant difference with regard to the food intake, gain in body weight and organ weights of rats in different dietary groups. RMR significantly lowered serum and hepatic cholesterol and triacylglycerol levels. LDL-C levels decreased by 66.28 and 70.12%, while HDL-C increased by 44.45 and 34.58% in serum of 16% RMR fed groups for 7 and 14 weeks, respectively. The atherogenic indices (LDL-C/HDL-C and TC/HDL-C) of 16% RMR for 14 weeks were reduced by 77.80 and 61.05%, respectively. RMR fed groups resulted in 22 to 54% inhibition of HMG-CoA reductase activity in liver. Further, the hypolipidemic effect of RMR was comparable to therapeutic drug lovastatin. In addition, histological examinations of liver of hyperlipidemic rats showed decreased lipid accumulation in red mould rice powder fed rats.

RMR effectively scavenged 2, 2-diphenyl-1-picrylhydrazyl (DPPH) radicals ($IC_{50}=100\mu\text{g/ml}$). The consumption of RMR with HFD showed increased enzyme activity (glutathione reductase, glutathione peroxidase, superoxide dismutase and catalase) and increased levels of non-enzymic (total thiols, glutathione and ascorbic acid) antioxidants in rats. Lipid peroxidation was significantly inhibited in rats ($46\mu\text{mol/dl}$) fed on RMR compared to rats fed on HFD only ($99\mu\text{mol/dl}$). The treatment of 16% RMR is equivalent to 80mg of lovastatin. This study has confirmed that, consumption of RMR can induce antioxidant enzymes and molecules to scavenge the reactive oxygen species (ROS) released due to oxidative stress in rats fed on HFD.