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Review Article

MONASCUS FERMENTED RICE AND ITS BENEFICIAL ASPECTS: A NEW REVIEW

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ABSTRACT

Monascus fermented rice has been traditionally used as a natural food colorant and food preservative of meat and fish for centuries. *Monascus* fermented products gradually regarded as the functional food because the monacolin K (antihypercholesterolemic agents), γ-aminobutyric acid (GABA) (hypotensive agent), and dimerumic acid (antioxidant) were found. This review article describes about the History and traditional use of *Monascus* fermented rice, Fermentation conditions for pigment production and Pharmacological aspects which include effects in cholesterol lowering, Anti-Diabetic Activity, Anti-Inflammation and prevention of Osteoporosis.

Key words: *Monascus purpureus*, Pigments, Solid State Fermentation, Pharmacological effects, Red Yeast Rice (RYR).

INTRODUCTION

Microorganisms are known to produce pigments, among them, the fungi *Monascus purpureus* is one such agent that produce a variety of pigments which posses several beneficial aspects to humans. The pigments produced by *Monascus* are considered as the most important agent, which have been used for centuries as food colorant in Eastern countries. *Monascus purpureus* is one of the red mold rice species which may be cultivated on starch containing substrates .The solid state fermentation of rice by *Monascus* has a long tradition in East Asian countries which dates back at least to the first century A.D. For centuries *Monascus* fermented rice products in the name of Red Yeast Rice (RYR) have been consumed in Asia and Indonesia as dietary staples and food additives. *Monascus* was classified and named in 1884 by French scientist Van Tieghem (1884). In 1895, Went published a careful study on *Monascus purpureus*, a species discovered from the samples collected by Dutch scientists in Java, where it was used largely for coloring rice. The Genus *Monascus* belongs to the family Monascaceae, the order Eurotiales, the class Ascomycetes, the phylum Ascomycota, and the kingdom Fungi[1]. *Monascus*-fermented product was gradually regarded as the functional food because the monacolin K (antihypercholesterolemic agents), γ-aminobutyric acid (GABA) (hypotensive agent), and dimerumic acid (antioxidant) were found [2,3]

HISTORY AND TRADITIONAL USE

The solid state fermentation of rice by *Monascus purpureus* has a long tradition in East Asian countries which dates back at least to the first century A.D. [4]. In China RYR is called as *angkak.* In ancient time, *angkak* production was originated in China and kept as a secret, but it has been used for Chinese cheese preparation and Chinese beverage known as *Anchu.* Later, one report suggested that *angkak* was used in the Philippines for coloring of bagoong, atsike salted fish, and in the preparation of alcoholic beverages such as *anchu* and *somsu.* In addition, angkak in the form of cake or ground red powder was exported from China to Eastern Asia. At present, several countries produce *angkak* both for internal use and export as food additive and dietary supplement[5]

In Japan Red Yeast Rice is known as *beni-koji* and its pigment is widely used as food coloring agent. Red yeast rice has also been used in China, Taiwan, Okinawa, and the Philippines as a preservative for meat and fish, for ensure color and aroma to food, and even for brewing wine and liquor. Interestingly, red yeast rice is also mentioned in an ancient Chinese pharmacopoeia of medicinal foods and herbs, the Ben Cao Gang Mu of Li Shi-zhen, where it is described as a medication useful for improving digestion and revitalizing the blood[6].

Red Yeast Rice obtained from *Monascus* has been widely used in China in dual ways such as dietary purpose and also as a medicinal substance. Manufacturing procedures of red yeast rice were described in addition to the therapeutic activities, including the betterness of digestion and revitalizing the blood circulation[7].

Angkak were also found to posses many pharmaceutical aspects. It was already published during the Ming Dynasty (A.D 1368-1644), described with the medicinal function of *angkak* for the treatment of indigestion and diarrhea, bruised muscles, hangovers and colic dyspepsia in children. Besides, it has been used for improving blood circulation and for promoting the function of the spleen and stomach. Moreover, several books including *Materia Medica for Daily Use*, *Supplements on Developments of Herb Medicine*, and *Compendium of Material Medica* also described the utilization of this pigment as a coloring agent and in medicine for the treatment of various diseases.

PIGMENTS OF *M. PURPUREUS*

Pigments are produced mainly in the cell-bound state. A few examples are the orange pigments such as monascorubin and rubropunctatin, which posses the oxolactone ring, the red pigments such as monascorubramine and rubropunctamine, which are the yellow pigment such as monacin and ankaflavin[8].

Monascus fungi produce at least six major related pigments which can be categorized into 3 groups based on color. The red colorants named rubropunctamine ($C_{21}H_{23}NO_4$) and monascorubramine ($C_{23}H_{27}NO_4$) are most abundant. The orange colorants are rubropunctatin ($C_{21}H_{22}O_5$) and monascorubrin ($C_{23}H_{26}O_5$). The yellowish colorants are monascin ($C_{21}H_{26}O_5$) and ankaflavin ($C_{23}H_{30}O_5$). Moreover, a yellowish colorant named Xanthomonasin A in the mutant of *Monascus anka* was identified (Martinkova *et al.*, 1999). Although for years it has been known that there are six pigments, in the last decade some new pigments have been discovered, which included xanthomonascin and yellow II, possibly derived from rubropunctatin[9,10,11].

FERMENTATION CONDITIONS FOR PIGMENT PRODUCTION

Generally, pigment production in industrial scale has been carried out using submerged fermentation (SmF). However, solid-state fermentation (SSF) systems appear to be promising due to the natural potential and advantages they offer[12.] Carbon and nitrogen sources are nutritional sources required for mycelial growth. Generally, glucose is considered as the best carbon source for formation of pigment[13].

The difference in pigment formation when glucose and ethanol are used as carbon sources, and found out that ethanol has better pigment formation ability when it is used as carbon sources similar to starch, maltose, sucrose, and galactose.[14,15,16] .

The nitrogen source such as ammonium and peptone gave superior growth and pigment concentration is achieved at greater rate. *Monascus* growth and ankaflavin synthesis were favored at low pH (pH 4.0) whereas production of other pigments was relatively independent of pH[17]. In addition, ammonium chloride, sodium

nitrate, peptone, and monosodium glutamate also posses different effects on metabolite formation[18].

Monascus pigments are unstable towards light probably due to rapid degradation of secondary metabolites .Degradation of red pigment was comparatively faster above pH 8.0 or below pH 4.0. A good pH stability of *Monascus* pigment could be achieved by maintaining pH in the range from 6.0 to 8.0 by addition of the appropriate buffers and or solvents[19].

The potential of jack fruit seed power as a substrate for *Monascus* pigment production by soild-state fermentation process was reported[20]. *Monascus purpureus*, can produce Monacolins K at 2,584 mg kg^{-1}, which is 5.37 times equalizes when rice is used as the substrate.

PHARMACOLOGICAL EFFECTS

Monascus-fermented product was gradually regarded as the functional food because the monacolin K (antihypercholesterolemic agents), γ-aminobutyric acid (GABA) (hypotensive agent), and dimerumic acid (antioxidant) were found[2,3].

Figure 1: *Monascus* Fermented Rice

Effects in Cholesterol Lowering

In the 1970s, *monacolin k*, an important metabolite of *Monascus sp*., was identified and shown to inhibit the synthesis of cholesterol. It was also shown to provide benefits to sufferers of cardiovascular disorders. The critical reaction in the pathway of cholesterol synthesis is the formation of mevalonic acid from 3-hydroxy-3 methylglutaryl CoA (HMG-CoA) by HMG-CoA reductase. *Monacolin k* is structurally similar to HMG-CoA and plays a role as a competitive inhibitor, which competes with HMG-CoA and reduces the synthesis of cholesterol[21, 22, 23,24].

There are 14 monacolin compounds identified such as monacolin K , J, L, M, X and their hydroxy acid form, such as dehydromonacolin K, dihydromonacolin L, compactin, 3α-hydroxy- 3,5-dihydromonacolin L, etc., were identified in Red Yeast Rice (RYR) by HPLC. One of these, "monacolin K", is a potent inhibitor of HMG-CoA reductase inhibitor, which is also known as mevinolin or lovastatin, a semisynthetic derivative now in use as cholesterol-lowering drugs[25]. RYR also contains unsaturated fatty acids that may also contribute in reducing the serum cholesterol level by lowering triglycerides [26].

Lovastatin, a hypocholestromic agent, competitively inhibit the rate-limiting enzyme HMG-CoA reductase, which catalyzes the reduction of HMG-CoA to mevalonate during cholesterol biosynthesis[21,27].

Monascus purpureus rice therapy reduced LDL-C by 27.7%, total cholesterol by 21.5%, triglycerides by 15.8% and apolipoprotein B by 26.0%. High-density lipoprotein cholesterol and apolipoprotein A-I levels were increased by 0.9 and 3.4% respectively.[28]

Effects In Anti-Diabetic Activity

Various studies also reported that red yeast rice and statins decreases blood glucose levels in diabetes. Aqueous extract of the fermented rice at two dose levels showed a significant decrease in fasting blood glucose level[29]. Flavonoids, phytosterols, and pyrrolonic compounds possess potential to reduce blood sugar and triglycerides levels while raising HDL-C. It is also found to be useful in treatment of metabolic syndromes[30].

Traditionally fermented red yeast rice proved to contain many active constituents such as compounds resembling statins in its structure, unsaturated fatty acid, sterols and B-complex vitamins[26].

Effects on Osteoporosis

A bone morphogenetic protein regulates the osteogenic differentiation during bone fracture repair. RYR extract contains several statin-like components that inhibit the HMG-CoA reductase. Statin-mediated activation of bone morphogenetic protein-2 Promoter was inhibited by mevalonate which is the downstream metabolite of HMG-CoA reductase. The effect of RYR extract on bone formation suggests that the inhibition of HMG-CoA reductase in the mevalonate pathway may increase bone cells. In recent study, it was found that RYR extract increases the osteogenic activity, cell viability, and mitochondrial activity[31].

Other uses

The certain composition of yellow pigment is identified as monascin, which has been shown as an Anti-Inflammatory agent exhibiting potent inhibitory effects on 12-Otetradecanoylphorbol-13-acetate (TPA)-induced inflammation in mice in previous studies[32].

GABA has been widely researched on its role of an inhibitory neuronal signal transmitter. The crude extract of MFR could alleviate hypertension in rats, a systematic fractionation and isolation of the responsible bioactive compound was conducted. Therefore, GABA and its pharmacological role to alleviate hypertension were discovered[33].

CONCLUSION

Red yeast rice is not only used as food colorant, flavoring agent and preservative it is widely applied in medicinal aspects. Apart from food coloring it has been used in clinical therapy to lower the blood cholesterol concentration, Anti-Diabetic Activity, Anti-Inflammation and prevention of Osteoporosis was proved.

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