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Rhodotorula Mucilaginosa: Two Faces of the Yeast

Tejpal Singh Parmar[1], Ragini Gothalwal[1], Sanjay Sahay[2*]

[1]Department of Biotechnology, Barkatullah University, Bhopal

[2]Sarojini Naidu Government Girls' PG College, Bhopal

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Abstract- *Rhodotorula mucilaginosa* (previously called *Rhodotorula rubra*) is basidiomycetous yeast of cosmopolitan distribution, from poles to equator, from soil to water and from plant to animal interiors including human gut. It contributes to immunity in animals, and plant, serves as industrial source of carotene and enzymes, and shows probiotic properties, plant growth promoting activities, and potential for bioremediations on the one hand, and furnishes evidences as being emerging pathogen in tested animals and immunocopromisd human beings on the other hand.

1. INTRODUCTION

Rhodotorula is a common basidiomycetous yeast that is found in air, soil, fresh and saline water [1], milk, and fruit juice [2]. The taxon *Rhodotorula* has eight species of which *R. mucilaginosa, R. glutinis, R. minuta* have been isolated from pathological lesions in human beings [2 ,3]. *R. mucilaginosa* (previously *R. rubra*) is the most highly distributed species among eight occurring from tropics to Polar Regions. It does colonise plants, humans, and other mammals. This species has been reported to form pink to red colonies, circular to oval cells, blastoconidia, and pseudohyphae. The colony may be butyrous (at or above 30^{o}C) or mucoid (at 20^{o}C or below). The anamorophic yeast has been reported to produce arthrospores at lower temperature [4]. Since 1985,

the number of infected persons caused by this yeast has increased substantially possibly due to advancement of medical science and the wider use of central venous catheters (CVCs) [5]. This yeast shows a affinity for plastic, and thus colonize plastic surface of surgical/medical devices such as dialysis equipment, plastic cathetars, fibre-optic bronchoscopes, and other personal objects such as bathtubs, shower curtains, and toothbrushes [2, 6].

2. BENEFICIAL ROLES

2.1. Probiotic

R. mucilaginosa has been reported from the gastrointestinal tract (GI) of wild fishes e.g. *Abramis brama*, *Rutilus rutilus*, *Perca fluviatilis* colonized permanently. The yeast could biosynthesis β-carotene, torulene, torularhodin, and exopolysaccharides (EPS) under fish GI condition and via this ability the yeast was involved in non-specific stimulation of immuno and antioxidative protection [7]. In case of apple this yeast has been reported to reduce the disease incidence caused by *Penicillium expansum*, the biocontrol impact was enhanced when the treatment was with yeast combined with phytic acid [8]. A marine isolate of *R. mucilaginosa* ZTHY2 was used to gavage experimental mice (200) to study its impact on the immune function and gut microbiota. The result showed an increase in the thymus and spleen indices of mice, the increase was more prominent with long term gavage administration (30 days) than short term one (15 days). Also short-term gavage administration while increased delayed hypersensitivity, serum IgG, IgA, and IL-2, long-term gavage administration enhanced the phagocytosis of macrophages and increased serum TNF-α and INF-γ. There was qualitative shift in gut microbiota as well; population of harmful bacteria Firmicutes was found to be reduced at the exppance of beneficial bacterium belonging to *Lactobacillus* [9].

2.2. Enzymes

Cold active enzymes from cold-adapted microorganisms have been of interest due to their immense industrial potential. The processing with cold active enzyme may not require exogenous energy thus save energy and consequently environment [10]. In case of food processing industries, cold active enzymes ensure preservation of nutritional quality and aromatic profile of the products as the process is done at low temperature [11]. The yeast has been studied with respect to its ability to produce aspartyl protease [12]. The amylase from this yeast was found to exhibit ethanol tolerance, maximum activity at a pH of 7.0 and at 60°C, and ability to saccharify corn starch [13]. The optimum pH and temperature were 4.0 and 70 °C for *R. mucilaginosa* invertase. Both the

enzymes showed good catalytic activity with 10% of ethanol in reaction mixture. The hydrolysis by invertases occurs predominantly when sucrose concentrations are ≤5%. On the other hand, the increase in the concentration of sucrose to levels above 10% results in the highest transferase activity, reaching about 13.3 g/L of nystose by *S. cerevisiae* invertase and 12.6 g/L by *R. mucilaginosa* invertase [14]. The red yeast yielded an esterase in response to induction with triacetin was found specific for substrates bearing an O-acetyl group. The enzyme was however able to act almost nonspecifically for the substrates bearing a phenol, a monosaccharide, a polysaccharide, or an aliphatic alcohol. The esterase showed higher activity against acetylxylan and glucose β-D-pentaacetate, exhibited Michaelis-Menten kinetics, maximal activity in pH range 8.0-10.0 and temperature stability for 2h at 55°C. Since the yeast did not produce xylanase, hence might serve as suitable source for acetylxylan esterase free of xylanolytic activity [15]. Immobilized inulinase (5%, w/v) on chicken eggshell was successfully used to produce fructooligosaccharides from inulin substrate solution. The maximal activity of this enzyme was 3.54 U at optimal pH 8.0 and temperature 75°C [16].

2.3. Food colorant

Bio-colorants are considered better than synthetic colors as former impart colour without any health hazard. Additional advantage with bio-colorants may be their antioxidants properties. *R. mucilaginosa* is known source of carotenoid, a red pigment. The yeast has been used to produce carotene under submerged fermentation using agro-industrial residues such as onion peels, potato skin, mung bean husk and pea pods. Maintaining the optimum conditions (pH 6.1, temperature 25.8 °C and agitation 119.6 rpm) more than 100 µg carotenoids per g of dry biomass could be produced, with the major carotenoid compounds being torularhodin, β-carotene, and torulene [17].

2.4. Nutrient

Oleaginous compounds such as lipids, carotenoids and fatty acids constitute one of the important classes of functional food. They serve as an energy source, antioxidants and metabolic agents for the human body. The isolate *R. mucilaginosa* CCT3892 has been studied with respect to its potential as source of functional food. The yeast was grown both in sugarcane molasses medium (MC) and synthetic medium; an equivalent yield of total lipids (16.5 % and 15.36 mg g^{-1}; and 0.053 and 0.051 mg g^{-1} respectively) and carotenoids was obtained. MC medium grown yeast also generated greater content of oleic acid (74.05%) vis-à-vis SC medium [18]. Polyunsaturated fatty acids (PUFAs) are highly beneficial functional food item for human beings especially with a cardiac problem. PUFA is not synthesized by human body, therefore an exogenous supply is essential.

Traditionally, Porcine liver and fish oil have been used as source of PUFA since long, a cheaper microbial source is highly desirable. Additionally, microbial oils are also useful as precursor of biodiesel. The yeast *R. mucilaginosa* has been studied with respect to the quality and quantity of lipids produced by it [19]. The endophytic isolate R. mucilaginosa JGTA-S1 has been reported to possess genes for carbohydrate catabolizing enzymes (CAZY families) e.g GH16 . GH16 enzymes hydrolyze ß-1, 3-1, 4-glucans found in the cell walls of grasses [20].

2.5. Growth promoting activities

Recently, the yeast isolate *R. mucilaginosa* JGTA-S1 has been isolated as an endophyte of *Typha angustifolia*. The yeast possess phosphate solublizing and phytohormones synthesizing ability and harbours nitrogen fixing bacterium. The yeast also contains anti-freezing genes that may be used to implant freezing resistance in crop plants [20].

3. HARMFUL ROLES

3.1. Fungemia (Rhodotorulosis)

R. mucilaginosa has been reported to cause skin infections in chickens, lung infection in sheep [21, 22], skin infection in a sea lion, and in a cat [23, 24]. The yeast has been isolated from the oropharynx and cloaca of ostriches, and the cloaca of wild birds and pigeons [25, 26]. Animal model rat has been used to study the pathogenesis-mechanism of this yeast. It has been found that rat showed severe infection in lungs, spleen, and in particular the liver characterized by the presence of some epithelioid cells, and multinuclear giant cells, and sometimes granuloma with abundant yeast cells in the vicinity [27]. In an Italian neonatal intensive care unit (NICU), four cases of CVC-related infection by *R. mucilaginosa* has been reported. All the infected newborns were premature, three previously infected with bacteria, and three had been administered fluconazole [28]. In another study on seven patients with Rhodotorulosis in a Brazilian hospital between 2002 and 2005, important predisposing factors with respect to this infection were cancer taking corticosteroids and cytotoxic drugs, use of central venous catheters, and broad-spectrum antibiotics [29]. Similar study with 25 fungemia patients by *R. Mucilaginosa* mostly with a CVC, and some (10 patients or 40%) with bone marrow transplantation was made. Four (17%) among them patients died [30]. Between 1966 and 2006, 66 patients with CVC-related fungemia were studied and found to be infected mostly by *R. mucilaginosa* [31]. Overall, the studies revealed *R.*

mucilaginosa to be emerging pathogen with the common predisposing factors are malignancies, AIDS, cirrhosis, and gastrointestinal disorders as well as the use of CVCs [32] and chronic renal problem [33]. In china, between 2009 and 2019, a hospital survey was made to study the significance of *R. mucilaginosa* in causing fungemia, their genotyping and genetic transmission of drug resistance. The data indicated possible clonal transmission of pan echinocandins-azoles-5-flucytosine resistance, and that the yeast exhibited multi-drug resistance and ability to cause nosocomial infection [34].

3.2. Food contaminants

R. mucilaginosa has been frequently reported from foods and beverages [35]. For example, this yeast has been isolated from peanuts, apple cider, cherries, fresh fruits, fruit juice, cheese, sausages, edible molluscs, and crustaceans [32, 35, 36]. Taking a food containing this yeast is not sure to cause opportunistic infections, yet an overload of this yeast inside gut may be of concern especially in the case of immunocompromized persons [2]. This yeast species is very common in air and on the surface of plastic equipments; these facts seriously expose the patients to infection by this yeast in the hospital. The ability to survive in the human gut again enhances the ability of the pathogenecity of this yeast.

4. Conclusion

R. mucilaginosa is now emerging an important pathogenic yeast for immunocompromized persons, and thus a proper therapeutic strategy has to be sought. Simultaneously, its probiotic potential and other biotechnological applications need to explored. The yeast has also been reported to exhibit plant growth promoting activities and genes coding for cellulases. These angles also need a concerted investigation for their suitable applications.

References

[1] D. Libkind, S. Brizzio, M. Van Broock, " *Rhodotorula mucilaginosa*, a carotenoid producing yeast strain from a Patagonian high-altitude Lake" *Folia Microbiologica*, vol.49, no. 1, pp. 19–25, 2004.
[2] H. Hof, "*Rhodotorula* spp. in the gut - foe or friend?" *GMS Infectious Disease*, vol. 2, no.7, pp. Doc02, September 2019.

[3] D.H. Larone, *Medically Important Fungi—A Guide to Identification*, 3rd edition, American Society for Microbiology, Washington DC, USA, 1995.

[4] S. Sahay, A.M. Khan, M. Butt, T. Sahu, R.S. Rana, D. Chouhan, K. Ranjan, B. Hamid, "*Rhodatorulla mucilaginosa* PT1 can form arthrospore in response to cold temperature" *Journal of Coastal Life Medicine*, vol. 2, no. 2, pp. 141-145, 2014.

[5] M.H. Miceli, J.A. Díaz, S.A. Lee, "Emerging opportunistic yeast infections" *The Lancet Infectious Diseases*, vol. 11, no. 2, pp. 142–151, 2011.

[6] T.E. Kiehn, E. Gorey, A.E. Brown, F.F. Edwards, D. Armstrong, "Sepsis due to *Rhodotorula* related to use of indwelling central venous catheters" *Clinical Infectious Diseases*, vol. 14, no. 4, pp. 841–846, 1992.

[7] E. Bogusławska-Wąs, A. Dłubała, M. Laskowska, "The role of *Rhodotorula mucilaginosa* in selected biological process of wild fish" *Fish Physiology and Biochemistry*, vol. 45, pp. 511–521, 2019.

[8] Q. Yang, H. Zhang, X. Zhang, X. Zheng, J Qian, "Phytic acid enhances biocontrol activity of *Rhodotorula mucilaginosa* against *Penicillium expansum* contamination and patulin production in Apples" *Frontiers in Microbiology*, vol. 6, 2015.

[9] G.Y. Liu, K. Huang, W. Xie, C. Xu, Q. Yao, Y Liu, "Effects of *Rhodotorula mucilaginosa* on the immune function and gut microbiota of mice. *Frontier in Fungal Biology*, vol. 2 pp. 705696, 2021. doi: 10.3389/ffunb.2021.705696

[10] S. Sahay, B. Hamid, P. Singh, K. Ranjan, D. Chauhan, R.S. Rana, V.K. Chaurse, "Evaluation of pectinolytic activities for oenological uses from psychrotrophic yeasts" *Letters in applied microbiology*, vol. 57, no. 2, pp. 115-121, 2013.

[11] D. Chouhan, S. Sahay, "Detergent compatible cold-active lipases from psychrotrophic fungi for cold washing" *Journal of Genetic Engineering & Biotechnology*, vol. 16, no. 2, pp. 319-325, 2018.

[12] L.D. Lario, O.S. Pillaca-Pullo, L. Durães Sette, A. Converti, P. Casati, C. Spampinato, A. Pessoa, "Optimization of protease production and sequence analysis of the purified enzyme from the cold adapted yeast *Rhodotorula mucilaginosa* CBMAI 1528" *Biotechnology Report (Amst)*, vol. 22, no.28, p. e00546, October 2020.

[13] A.P.A. de Oliveira, M.A. Silvestre, H.F. Alves-Prado, A. Rodrigues, M.F. da Paz, G.G. Fonseca, R.S.R. Leite, "Bioprospecting of yeasts for amylase production in solid state fermentation and evaluation of the catalytic properties of enzymatic extracts" *African Journal of Biotechnology*, vol. 14, no. 14, pp. 1215-1223, 2015.

[14] P.M.G. Barbosa, T.P. de Morais, C.A. de Andrade Silva, F.R. da Silva Santos, N.F.L. Garcia, G.G. Fonseca, R.S.R. Leite, M.F. da Paz, "Biochemical characterization and evaluation of invertases produced from *Saccharomyces cerevisiae* CAT-1 and *Rhodotorula mucilaginosa* for the production of fructooligosaccharides, *Preparative Biochemistry & Biotechnology*, vol. 48, no. 6, pp. 506-513, 2018.

[15] H. Lee, J.B.T. Rebecca, K.L. Roger, B. Peter, S. Hemry, "Some Properties of Extracellular Acetylxylan Esterase Produced by the Yeast *Rhodotorula mucilaginosa*" *Applied and Environmental Microbiology*, vol. 53, no. 12, pp. 2831-2834, 1987.

[16] G.C. deAraujo Ribeiro, P. Fernandes, D.A.A. Silva, H.N. Branda, S.A. de Assis, "Inulinase from *Rhodotorula mucilaginosa:* immobilization and application in the production of fructooligosaccharides" *Food Science and Biotechnology*, vol. 30, no. 7, pp. 959–969, 2021.

[17] R. Sharma, G. Ghoshal, "Optimization of carotenoids production by *Rhodotorula mucilaginosa* (MTCC-1403) using agro-industrial waste in bioreactor: A statistical approach" *Biotechnology Reports*, vol. 25, pp. e00407, March 2020.

[18] W.A. Costa, C.E.A. Padilha, S.D. Oliveira Júnior, F.L.H. Silva, J. Silva, M.A. Ancântara, M. Ferrari, E.S. Santos, "Oil-lipids, carotenoids and fatty acids simultaneous production by *Rhodotorula mucilaginosa* CCT3892 using sugarcane molasses as carbon source. *Brazilian Journal of Food Technology*, vol. 23, pp. e2019064, 2020.

[19] R. Jasmine, R. Ganesh, S. Mohanapriya, R. Dharani, "Probiotic rhodotorula mucilaginosa isolated from fermented food: investigation of pufa production and strategy for health improvement" *Asian Journal of Advances in Medical Science*, vol. 4, no.4, pp. 5-11, 2022.

[20] D. Sen, K. Paul, C. Saha, G. Mukherjee, M. Nag, S. Ghosh, A. Das, A. Seal, S. Tripathy, "A unique life-strategy of an endophytic yeast *Rhodotorula mucilaginosa* JGTA-S1—a comparative genomics viewpoint" Dna Research, vol., 0, no. 0, pp. 1–16, 2019.

[21] S.K. Aruo, "Necrotizing cutaneous rhodotorulosis in chickens in Uganda" *Avian Diseases* vol. 24, no. 4, pp. 1038–1043, 1980.

[22] D.P. Monga, D.N. Garg, "Ovine pulmonary infection caused by *Rhodotorula rubra*" *Mykosen*, vol. 23, no. 4, pp. 208–211, 1980.

[23] S. Alvarez-Perez, A. Mateos, L. Dominguez, E. Martinez-Nevado, J.L. Blanco, M.E. Garcia, "Isolation of *Rhodotorula mucilaginosa* from skin lesions in a Southern sea lion (*Otaria flavescens*): a case report" *Veterinarni Medicina*, vol. 55, no. 6, pp. 297–301, 2010.

[24] P. Bourdeau, B. Hubert, J.P. Magnol, "Suspicion de dermatomycose à *Rhodotorula mucilaginosa* chez un chat infecté par le FeLV et le FIV" *Recueil de Médecine Veterinaire*, vol. 168, no. 2, pp. 91–96, 1992.

[25] A.T.K. Lord, K. Mohandas, S. Somanath, S. Ambu, "Multidrug resistant yeasts in synanthropic wild birds" *Annals of Clinical Microbiology and Antimicrobials*, vol. 9, pp. 11, 2010.

[26] A.K.F. Costa, J.J.C. Sidrim, R.A. Cordeiro, R.S.N. Brilhante, A.J. Monteiro, M.F.G. Rocha, "Urban pigeons (*Columba livia*) as a potential source of pathogenic yeasts: a focus on antifungal susceptibility of *Cryptococcus* strains in Northeast Brazil" *Mycopathologia*, vol. 169, no. 3, pp. 207–213, 2010.

[27] F. Wirth, L.Z. Goldani, "Experimental rhodoturolosis in rats" *Acta Pathologica, Microbiologica et Immunologica*, vol. 120, pp. 231–235, 2012.

[28] R. Perniola, M.L. Faneschi, E. Manso E, "*Rhodotorula mucilaginosa* outbreak in neonatal intensive care unit: microbiological features, clinical presentation, and analysis of related variables" *European Journal of Clinical Microbiology and Infectious Diseases*, vol. 25, no. 3, pp. 193–196, 2006.

[29] L.W. Lunardi, V.R. Aquino, R. A. Zimerman, L.Z. Goldani, "Epidemiology and outcome of *Rhodotorula* fungemia in a tertiary care hospital" *Clinical Infectious Diseases*" vol. 43, no. 6, pp. e60–e63, 2006.

[30] G.M. Duboc de Almeida, S.F. Costa, M. Melhem et al., "*Rhodotorula* spp. isolated from blood cultures: clinical and microbiological aspects" *Medical Mycology*, vol. 46, no. 6, pp. :547–556, 2008.

[31] F.F. Tuon, G.M. Duboc de Almeida, S.F. Costa, "Central venous catheter-associated fungemia due to *Rhodotorula* spp.—a systematic review" *Medical Mycology*, vol. 45, no. 5, pp. 441–447, 2007.

[32] F. Wirth, L.Z. Goldani, "Epidemiology of *Rhodotorula*: an emerging pathogen" *Interdisciplinary Perspective Infective Disease* vol. 2012, pp. 465717, 2012.

[33] I.C. Jarros, F.F. Veiga, J.L. Corrêa, I.L.E. Barros, M.C. Gadelha, M.F. Voidaleski, N. Pieralisi, R.B. Pedroso, V.A. Vicente, M. Negri, T.I.E. Svidzinski, "Microbiological and virulence aspects of *Rhodotorula mucilaginosa*" *EXCLI Journal* vol. 2020, no. 19, pp. 687-704, 2019.

[34] J.-J. Huang, X.-F. Chen, C.K.M. Tsui, C.-J. Pang, Z.-D. Hu, Y. Shi, W.-P. Wang, L.-Y. Cui, Y.-L. Xiao, J. Gong, X. Fan, Y.X. Li, G. Zhang, M. Xiao, Y.-C. Xu, "Persistence of an epidemic cluster of Rhodotorulamucilaginosa in multiple geographic regions in China and the emergence of a 5-flucytosine resistant clone" *Emerging Microbes & Infections*, vol. 11, no. 1, pp. 1079-1089,2022.

[35] S. Senses-Ergul, R. Ágoston, A. Belák, T. Deák, "Characterization of some yeasts isolated from foods by traditional and molecular tests" *International Journal of Food Microbiology*, vol. 108, no. 1, pp. 120–124, 2006.

[36] F. Gardini, G. Suzzi, A. Lombardi A, et al., "A survey of yeasts in traditional sausages of Southern Italy" *FEMS Yeast Research*, vol. 1, no. 2, pp. 161–167, 2001.