

PRODUCT DEVELOPMENT AND
EVALUATION OF PROBIOTIC TABLET
FROM LOCALLY ISOLATED YEAST
SACCHAROMYCES BOULARDII FOR
STOMACH ACID TOLERANCE

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Doctor of Philosophy

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SUPERVISOR'S DECLARATION

I hereby declare that I have checked this thesis and in my opinion, this thesis is adequate in terms of scope and quality for the award of the degree of Doctor of Philosophy.

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STUDENT'S DECLARATION

I hereby declare that the work in this thesis is based on my original work except for quotations and citations which have been duly acknowledged. I also declare that it has not been previously or concurrently submitted for any other degree at Universiti Malaysia Pahang or any other institutions.

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ABSTRAK

Mikroorganisma seperti bakteria, yis atau kulat yang hidup di saluran pencernaan dapat disebut sebagai microbiota usus atau probiotik. Mikroorganisma ini berperanan penting dalam mengekalkan kesihatan dan fungsi microbiota manusia. Produk probiotik diaplikasikan secara oral dan boleh didapati secara komersial dalam pelbagai bentuk, seperti produk makanan atau dalam bentuk dos farmaseutikal. Namun, setiap produk harus mempunyai daya tahan yang tinggi semasa proses pembuatan untuk mencapai kesan yang baik tanpa kehilangan kebolehidupan melalui proses penyimpanan atau pencernaan gastrik. Oleh itu, penyelidikan ini bertujuan untuk melibatkan pengasingan dan pengenalpastian potensi yis probiotik daripada sampel minuman kefir tempatan, memformulasi tablet probiotik dan menilai prestasi tablet untuk toleransi asid gastrik. Daripada proses pengasingan, sembilan spesis yis yang berbeza telah berjaya dikenalpasti. Yis *Saccharomyces boulardii* dipilih berdasarkan hasil yang paling positif dari proses penyaringan. Pemilihan ini dibuat berdasarkan kemampuannya untuk hidup pada pH rendah, dapat hidup dengan baik pada kepekatan garam hempedu yang tinggi, pertumbuhan optimum pada suhu badan manusia, dan dapat mencegah pertumbuhan bakteria patogen tertentu. 10% susu skim telah dipilih sebagai agen pelindung pembekuan untuk manambahbaik kebolehidupan sebanyak 40% semasa proses penyejuk-keringan. Dalam kajian ini, kaedah campuran simplex menggunakan perisian kajian rekabentuk dilaksanakan untuk menilai kesan biopolimer sebagai bahan pengikat atau eksipien. Kombinasi terbaik yang diperolehi melalui analisis perisian menunjukkan nisbah eksipien sebanyak 39.01% CMC dan 60.99% alginat berdasarkan peratusan kebolehidupan mikroba lebih tinggi dan masa tablet yang lebih rendah. Kedua-dua kombinasi ini menghasilkan toleransi terhadap asid yang lebih baik untuk tablet yang mengandungi strain *Saccharomyces boulardii*. Berdasarkan rumusan ini, nilai tindak balas yang diramalkan terhadap kebolehidupan mikroba iaitu 95.36% dan masa pembubaran iaitu 1.3 jam. Di samping itu, didapati tablet probiotik yang diformulasikan lebih stabil dari segi kebolehidupan dimana pengiraan sel hidup berkurang hanya sebanyak 0.22 log CFU apabila disimpan dalam suhu sejuk iaitu 4.0 °C berbanding pengurangan sebanyak 0.57 log CFU apabila disimpan pada suhu bilik iaitu 25.0 °C. Kajian ini boleh membawa kepada pengembangan pengeluaran komersial tablet yis probiotik dengan toleransi asid perut yang tinggi kerana formulasi ini boleh di pertimbangkan sebagai efektif, menggunakan kos yang rendah dan proses yang ringkas dengan membandingkan kepada produk komersial dalam pasaran.

ABSTRACT

The microorganisms such as bacteria, yeast, or fungi that live in the gastrointestinal tract can be referred to as gut microbiota or probiotics. These microbial associates play a significant role in maintaining the diversity and proper functioning of our gut microbiota and human health in many aspects. Probiotic products are orally consumed and commercially available in various forms, such as food products or pharmaceutical dosage forms. However, every product containing live cells should survive in the manufacturing process to achieve a beneficial effect without losing viability via the storage or gastric digestion process. Therefore, the aim of the present work involves the development of probiotic formulation using a simple and less step of the manufacturing process but effectively tolerate to human stomach acid. This work involves isolation and identification of potential probiotic cells from locally kefir drink samples, probiotic tablet formulation, and evaluate the tablet performance for gastric acid tolerance. From the isolation process, nine different yeast species were successfully identified. *Saccharomyces boulardii* was selected based on the yeast screening process's most positive result. This selection was made because of its ability to grow at low pH, can grow well in the high concentration of bile salt present in the medium, optimum growth at human body temperature, and can suppress certain pathogenic bacteria. In the lyophilization process, skim milk 10% was selected as a cryoprotectant agent to improve cell survivability up to 40% in the freeze-drying process. In this study, a simplex-centroid mixture design using Design of experiment (DOE) was implemented to evaluate the effect of biopolymers as an excipient, and the best combination obtained with higher microbial viability and lower dissolution time only required 39.01% CMC and 60.99% alginate for the excipient ratio based on the software analysis. These two combinations produce better acidic tolerance for the tablet containing *Saccharomyces boulardii* strain. Under this formulation, the predicted response values were expected to obtain microbial viability of 95.36% and dissolution time of 1.3 h. In addition, it is found that the formulated probiotic tablet is more stable in terms of viability where the viable cell count reduces only 0.22 log CFU when stored in cold temperatures which are 4.0 °C compared to a reduction of 0.57 log CFU in room temperature which is 25.0 °C over 24 weeks of storage time. This study can lead to the development of commercial production of probiotic yeast tablets with gastrointestinal tolerance because this formulation can be considered as effective, low cost, and less step by comparing with the commercial product in the market.

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