Potential Combination of Probiotic Lactobacillus reuteri Encapsulated High Internal Phase Emulsion (HIPE)-Alginate and Modulation of Thylakoid-Based Prebiotic Diets: Alternative Prevention Strategies for Atherosclerosis

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BACKGROUND

Atherosclerosis is characterized by an atheroma that lines the vascular lumen and is highly susceptible to thrombosis and obstruction of tissue perfusion, which subsequently causes ischemia. This condition plays a significant role in the development of peripheral, cerebral, and coronary artery diseases. Atherosclerosis has one of the highest morbidity and mortality rate amongst all cardiovascular diseases globally. The existing long-term preventive measures are considered less than optimal, due to their cost, numerous significant side effects, and the patients' increasingly high demand for natural options in healthcare. Accordingly, utilization of probiotic and prebiotic agent as a preventive approach and/or definitive treatment has been developed, seeing its promising potential, low cost, and minimal side effect.

Aim of the review

To investigate the potential of the combination of HIPE-alginate encapsulated **probiotic *L. reuteri*** with **thylakoid-based diet** modulation as a preventive measure against atherosclerosis.

METHODS

Literature search

The literature search was carried out from December 2021 to January 2022 using online-based scientific journal databases including **Science Direct, PubMed, and Cochrane Library**

Keywords

The main keywords used in this review were atherosclerosis; anti-atherogenesis; anti-dys-lipidemia; anti-cholesterol; prebiotic; thylakoid; probiotics; lactobacillus reuteri; high internal phase emulsion; alginate.

Online databases

ELSEVIER PubMed Cochrane Library

Inclusion criteria

The inclusion criterias used in this review are **(1)** publication of the last 10 years; **(2)** written in English or Indonesian.

48 suitable studies were obtained as the main references. All studies were then critically reviewed in terms of **validity, importance, and applicability.** The types of data obtained are both qualitative and quantitative, thus may be compared and further analyzed.

RESULT & DISCUSSION

Lactobacillus reuteri and Its Anti-atherogenic Effect

Lactobacillus sp. is a part of human's gut microflora without pathogenic tendencies. *L. reuteri* in particular has been found to possess anti-atherosclerotic effect through the anti-cholesterol and anti-inflammatory pathways. This strain shows the highest potential compared to other *Lactobacillus* species. In addition, *L. reuteri* has competitive advantage in its resistance and maintenance in the gastrointestinal tract. However, exposure to gastric acid and bile salts can significantly reduce the life span of these bacterias.

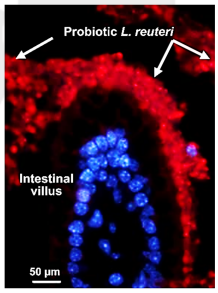

Figure 1. Human-derived L. reuteri 17938 using Cy3-conjugated probe (red) (Preidis et al, 2012)

Table 1. Previous studies of L. reuteri effects on lipid profile of atherogenic model population

Author, Year	Strain *L. reuteri*	Doses	Effects
Huang, 2015	263 (Lr263)	Human: 900 mg/day (lyophilized powder) or 2.1 ×10^9 cells/serving/day.	↑ HDL-C and ↓ TC, TG, LDL-C, LDL-C/HDL-C ratio, hepatic TC
Singh, 2015	LR6	Rat: 10^8 CFU/mL for 60 days	↓ TC, TG, and LDL
Jones, 2012	NCIMB 30242	Human: 2.9 x 10^9 CFU per capsule for 9 weeks	↓ LDL-C by 11.64%, TC by 9.14%, non-HDL-C
Yang, 2021	FYNLJ109L1	Mice: 5 × 10^9 CFU/mL for 14 weeks	↓ LDL-C and LDL-C/HDL-C
Lu, 2022	Fn041	Mice: 1 × 10^9 CFU/day for 8 weeks	↓TC and LDL-C
Sun, 2020	HI120	Mice: 1.000 mg/kg daily (every 2 days after 8 weeks) for 12 weeks	↓ TC
Ting, 2015	GMNL-263	Hamster: 2,5 × 10^9 cells/kg per day for 8 weeks	↓ LDL-C and TC

Thylakoid and Its Anti-atherogenic Effect

Thylakoid, a component in chloroplast with functions related to photosynthesis, was discovered to affect atherosclerosis positively through fat emulsification, antioxidant pathway, and activation of peroxisome proliferator-activated receptors (PPARs). This substance may also act as a prebiotic, sustaining the survival and growth of *L. reuteri* in the gut by regulating appetite and food consumption.

Potential Combination of *L. reuteri* (Probiotic) and Thylakoid-based diet (Prebiotic)

L. reuteri and thylakoid have anti-atherogenic effects through bile-salt hydrolase enzyme secretion mechanism, immunomodification effect, regulation of cholesterol absorption, production of short chain fatty acids, increased antioxidant activity, inhibition of HMG-CoA reductase, and regulation of gut microbiota through the prebiotic effect of thylakoids. *L. reuteri* was found to have a significant increase in the ileal mucosa of experimental animals fed thylakoid compared to controls.

High Internal Phase Emulsion (HIPE)-alginate Encapsulation

HIPE-alginate encapsulation aims to increase the viability of probiotics in the gastrointestinal tract. HIPE refers to the process of forming an emulsion with an internal phase volume fraction of >74%. Compared to other polymeric compounds such as chitosan, alginate-based encapsulation has a significant protective effect in aiding the administration of probiotic and is non-toxic.

CONCLUSION

The combination of probiotics and prebiotics, especially *L. reuteri* with dietary thylakoids was reported to have a significant anti-atherogenic effect. In addition, encapsulation using HIPE-alginate in *L. reuteri* preparations was reported to increase the viability of probiotics and provide protection against low pH conditions in the stomach when given orally.

LIMITATIONS

This review lacks studies that reported the mechanisms and interactions between probiotics and prebiotics. Thus, the safety and effectiveness of this combination therapy require further testing and investigations, especially in human clinical trials.

MAIN REFERENCES

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