PENGARUH Lactococcus lactis D4 TERHADAP HISTOPATOLOGI DAN INDEKS PROLIFERASI Ki-67 KOLON PADA TIKUS Sprague Dawley MODEL KANKER KOLOREKTAL TERKAIT KOLITIS

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ABSTRAK

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Pendahuluan: Kanker kolorektal terkait kolitis adalah komplikasi inflamasi kronis yang meningkatkan risiko karsinogenesis. Peningkatan kasus didunia maupun di Indonesia menjadi suatu permasalahan. Probiotik seperti *Lactococcus lactis* D4 berpotensi sebagai terapi pencegahan untuk colitis yang sel-selnya mengalami dysplasia.

Tujuan: Mengevaluasi efek *Lactococcus lactis* D4 terhadap histopatologi kolon dan indeks proliferasi Ki-67 pada tikus *Sprague Dawley* model kanker kolorektal terkait kolitis yang diinduksi *azoxymethane* (AOM) dan *dextran sodium sulfate* (DSS).

Metode: Penelitian ini merupakan penelitian eksperimental dengan pendekatan post-test only control group design. Sebanyak 18 tikus *Sprague Dawley* diadaptasikan selama 7 hari, kemudian dibagi menjadi tiga kelompok: kontrol negatif, kontrol positif (induksi AOM + DSS), dan perlakuan (induksi AOM + DSS serta *Lactococcus lactis* D4 secara rektal). Pada minggu ke-17, tikus diterminasi, jaringan kolon diperiksa dengan hematoxylin-eosin (HE) untuk histopatologi dan imunohistokimia untuk indeks Ki-67. Analisis data dilakukan menggunakan ANOVA dan LSD post-hoc dengan $p<0,05$.

Hasil: penelitian menunjukkan perbaikan histopatologi kolon yang signifikan, termasuk penurunan ketebalan mukosa, jumlah sel inflamasi, dan dysplasia pada kelompok perlakuan. Ekspresi Ki-67 pada kelompok perlakuan juga secara signifikan lebih rendah dibandingkan kontrol positif ($p<0,05$).

Kesimpulan: pemberian *Lactococcus lactis* D4 secara rektal mampu mengurangi kerusakan histopatologi kolon dan menurunkan indeks proliferasi Ki-67 pada tikus model CAC, menunjukkan potensi sebagai agen terapeutik tambahan.

Kata Kunci: *Lactococcus lactis* D4, kanker kolorektal, *colitis-associated cancer*, histopatologi kolon, Ki-67.

ABSTRACT

THE EFFECT OF *Lactococcus lactis* D4 On HISTOPATHOLOGY AND Ki- 67 PROLIFERATION INDEX OF THE COLON IN *Sprague Dawley* RATS MODEL OF COLITIS ASSOCIATED COLORECTAL CANCER

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Background: *Colitis-associated colorectal cancer (CAC) is a complication of chronic inflammation that significantly increases the risk of carcinogenesis. The rising incidence globally and in Indonesia poses a considerable challenge. Probiotics such as Lactococcus lactis D4 have the potential to serve as a preventive therapy for colitis characterized by dysplastic cell changes.*

Objectives:*This study aimed to evaluate the effects of Lactococcus lactis D4 on colon histopathology and Ki-67 proliferation index in a Sprague Dawley rat model of CAC induced by azoxymethane (AOM) and dextran sodium sulfate (DSS).*

Methods: *This research employed a laboratory experimental design with a post- test-only control group approach. Eighteen Sprague Dawley rats were acclimated for seven days and divided into three groups: negative control, positive control (AOM + DSS induction), and treatment (AOM + DSS induction followed by rectal administration of Lactococcus lactis D4). At week 17, the rats were sacrificed, and colon tissues were examined using hematoxylin-eosin (HE) staining for histopathology and immunohistochemistry for Ki-67 index. Data analysis was performed using ANOVA and LSD post-hoc tests with a significance level of $p<0.05$.*

Results: *The findings revealed significant improvements in colon histopathology in the treatment group, including reduced mucosal thickness, inflammatory cell counts, and dysplasia. Ki-67 expression was also significantly lower in the treatment group compared to the positive control ($p<0.05$).*

Conclusion: *In conclusion, rectal administration of*

Lactococcus lactis D4 effectively reduces colon histopathological damage and lowers the Ki-67 proliferation index in a CAC rat model, demonstrating its potential as an adjunctive therapeutic agent.

Keywords: *Lactococcus lactis D4, colorectal cancer, colitis-associated cancer, colon histopathology, Ki-67.*