P-ISSN: 2304-3075; E-ISSN: 2305-4360
International Journal of Veterinary Science
www.ijvets.com; editor@ijvets.com

Short Communication https://doi.org/10.47278/journal.ijvs/2024.165

Bdellovibrio bacteriovorus: A Boost for Hematological and Gut Health in Salmonella enteritidis-Infected Mice

Rondius Solfaine[1], Muhammad Thohawi Elziyad Purnama[2], Salipudin Tasil Maslamama[3], Faisal Fikri[4] and Iwan Sahrial Hamid[2*]

[1]Department of Pathology, Faculty of Veterinary Medicine, Universitas Wijaya Kusuma Surabaya, Surabaya, 60225, Indonesia
[2]Department of Basic Veterinary Science, Faculty of Veterinary Medicine, Universitas Airlangga, Surabaya, 60115, Indonesia
[3]Department of Agricultural Biotechnology, Faculty of Agriculture, Eskişehir Osmangazi Üniversitesi, Eskişehir, 26040, Turkey
[4]Department of Veterinary Anatomy, Faculty of Veterinary Medicine, Universitas Airlangga, Surabaya, 60115, Indonesia
***Corresponding author:** iwan-s-h@fkh.unair.ac.id

Article History: 24-435	Received: 07-Feb-24	Revised: 12-Apr-24	Accepted: 21-Apr-24	Online First: 27-Apr-24

ABSTRACT

Bacteria in the environment are naturally the target of predators, including various types of prokaryotes. This study aims to determine the effect of feeding *Bdellovibrio bacteriovorus* (Bb) isolate against *Salmonella enteritidis* (SE) inoculation in intestinal villi of mice models. Sixteen mice were used and were divided into 4 groups, namely the control with placebo (D0), the SE (D1), the SE+Tiamphenicol (D2), and the SE+Bb inoculation group (D3). Inoculation of SE was carried out intraperitoneally at a dose of $2.5x10^8$ CFU, and B bacteriovorus feeding treatment was given orally as a single dose containing $1x10^7$ CFU. On the 5th day post-treatment, all groups were euthanized, and blood samples were taken for examination of the hematological profiles in intestinal organs. Data analysis was performed using one way ANOVA test and Duncan's post hoc test ($P<0.05$). The results showed that there was a significant increase in the D3 group for the variables of leukocytes, lymphocytes, and neutrophils. Histomorphology analysis indicated that feeding of isolate inhibited the destruction of epithelia and enterocytes in duodenal tissue. Consequently, it was concluded that feeding of *Bdellovibrio bacteriovorus* can improve hematological value and the proliferation of villus in the intestine in SE-inoculation mice.

Key words: Health, Environment, Salmonella sp, *Bdellovibrio bacteriovorus, Salmonella enteritidis, Predator-prey interaction, Intestinal health, Hematological profiles*

INTRODUCTION

A variety of microorganisms are known to co-exist in the microbiological ecosystem, including predatory and pathologic prokaryotic germs. Some bacteria in the environment are natural targets of several types of bacteriophages and protists (Herencias et al. 2020). Previously studied that predators of bacteria are a group of organisms that are potential and beneficial in balance in the germ environment. One of the important aspects in the process of predation of germs is the release of nutritional compounds and biochemical phases in nature. Predatory germs have the ability to reduce the population of their target germs in low numbers, so the activity of predatory germs is very effective and efficient because they only need a small amount of their living medium (Mu et al. 2020).

Predatory bacteria, distinct from viruses and smaller than their prey, employ a variety of strategies to attack their host, for example, myxococci attack collectively but do not require direct physical attachment with their target germs (Negus et al. 2017; Liu et al. 2023).

These bacteria during various activities release several hydrolytic enzymes that destroy their target germs, to obtain nutrients. Another method used by epibiotic predatory germs, such as *Vampirococcus* is by attaching to the outer surface of prey cells, hydrolyzing and consuming the host. Meanwhile, the predatory *Bdellovibrio*-and-like-organisms (BALOs) infiltrate the periplasmic space of their prey germs (Kaljević et al. 2021; Ibrahimi et al. 2023).

Bdellovibrio bacteriovorus is a Gram-negative bacterium that is a predator against other germs, so this germ has the potential to be an alternative to antibiotics. Studies with intrarectal inoculation of BB germs in rats did not show any damage to colonic tissue and marked mild increases in pro-inflammatory cytokines for 24 and 48 hours after inoculation (Shatzkes et al. 2017). The interaction of

Cite This Article as: Solfaine R, Purnama MTE, Maslamama ST, Fikri F and Hamid IS, 2024. *Bdellovibrio bacteriovorus*: a boost for hematological and gut health in *Salmonella enteritidis*-infected mice. International Journal of Veterinary Science 13(6): 776-781. https://doi.org/10.47278/journal.ijvs/2024.165

Bdellovibrio bacteriovorus PF13 with Gram-negative bacteria (Pseudomonas fluorescens and Klebsiella pneumoniae) and Gram-positive (*Staphylococcus aureus* and *Enterococcus faecium*), showed an increase in the concentration of Bb PF13, which means that Gram-positive bacteria did not affect the predation efficiency of PF13 (Waso-Reyneke et al. 2022).

Bdellovibrio bacteriovorus, a predatory bacteria has two life cycles, the first involves attacking the target cell in the form of a vibrio with a single polar flagellum, and once within the target cell, the bacteria reside in the intra-periplasm space. In the second phase, the bacteria develop into non-flagellate circular non-septate filaments and shortly before leaving the damaged target cell undergo septation to produce many motile flagellated offspring which start a new cycle (Hobley et al. 2020; Odooli et al. 2020).

Bdellovibrio bacteriovorus is a small predator capable of killing and digesting other gram-negative bacteria in soil and aquatic environments. The ability to kill pathogens that are resistant to antibiotics, is by secreting various enzymes that lyse other pathogens. Predatory germs express only surface epitopes and transport proteins for host immune recognition (Cavallo et al. 2021). With dimensions of 0.2-0.5×0.5-2.5µm, *Bdellovibrio bacteriovorus* possesses small gram-negative properties discovered by scientists who isolated bacteriophages for plant pathogenic bacteria from soil (Im et al. 2018). These bacteria, which can be isolated from various habitats including both aquatic and terrestrial are predatory towards other germs, resulting in their use as an antibacterial agent across industries, agriculture and medicine. Several studies have been conducted to determine the nature of this predatory bacterium encompassing its life cycle, strategy to penetrate host cells, periplasmic growth, and distribution in the environment (Bonfiglio et al. 2020; Lowry et al. 2022). Based on the nature of *Bdellovibrio bacteriovorus* as a predator of certain germs, the possibility of applying this bacterium against plant pathogens and reducing contamination in the food industry has been explored (Bratanis et al. 2020; Youdkes et al. 2020). *Bdellovibrio bacteriovorus* is known as a germ that has a unique ability to prey on other Gram-negative bacteria. Today the problem of antibiotic resistance is increasing, BB bacteria have the potential to be effective probiotic agents and antibiotics. Many studies have been conducted on B. bacteriovorus to determine the basic aspects of its biology, intracellular life cycle, resistance and potential applications. The use of B. bacteriovorus as a live antibiotic for human therapy has been carried out with an in vivo model (Bukowska-Faniband et al. 2020).

Salmonella infection is one of the causes of serious and dangerous infections that attack humans and animals. Direct contact with infected animals or products is one way of transmission. Salmonellosis disease causes many losses in terms of medical costs, decreased productivity, and high mortality rates in livestock and poultry. Due to the problem of antibiotic resistance in many germs, including salmonella, studies on the use of probiotics and predatory germs have been conducted to provide appropriate and effective therapy for bacterial infections in animals and humans (Mazkour et al. 2020; Du et al. 2024). Therefore, this research purposed to analyze the effect of *Bdellovibrio bacteriovorus* (Bb) isolate against *Salmonella enteritidis* (SE) inoculation in intestinal villi of mice models.

MATERIALS AND METHODS

Research Design

This research was conducted in the Animal Experiment Laboratory, Faculty of Veterinary Medicine, Airlangga University, Surabaya. The research was conducted in accordance with ethical guidelines and approved by the Experimental Animal Ethics Commission No. 83–KKE of Universitas Wijaya Kusuma Surabaya, Indonesia the animals used were mice (*Mus musculus*) with inclusion criteria aged 2-3 months, weighing 30-40g. Animals were fed mice pellets, drank distilled water *ad libitum*, and reared for a week for adaptation. The treatment groups were inoculated with SE at a dose of $2.5x10^8$ (NCTC 12964, Intralab). The B. bacteriovorus isolate (NCTC 15356, USA) was prepared for experimentation by culturing in a nutrient-rich medium. Specifically, the culture medium consisted of nutrient broth (NB) supplemented with 2.4g/L of nutrient broth and 1.5g/L of yeast extract (YE), along with 1.5g/L of agar to solidify the medium. This standardized culture protocol ensured optimal growth conditions for Bdellovibrio bacteriovorus, allowing for the isolation and maintenance of the bacterium in the laboratory setting.

The experimental group comprised four Mus musculus mice, which were divided into four subgroups for the study. These subgroups included a control group administered with a placebo (D0), a group inoculated with Salmonella enteritidis (SE) (D1), a group inoculated with SE and treated with Tiamphenicol (D2), and a group inoculated with SE and treated with B bacteriovorus (D3). All treatment groups (D1, D2, and D3) were injected SE at dose of $2.5x10^8$ intraperitoneally, while group D3 was fed *Bdellovibrio bacteriovorus* at dose $1x10^7$ CFU/gr orally. All mice were sacrificed by cervical dislocation to collect intestinal duodenum samples for histological analysis on the eighth day. Tissue in area of duodenal slices were incubated with 10% neutral buffered formalin, blocked in paraffin, then cut ±3-5mm thick with a microtome and stained with hematoxylin-eosin (HE).

Duodenum villus histopathology was inspected in the regions altered such as infiltration cells, and necrotic cells under an Olympus light microscope (400x magnifications). The proportion of tissue area with alteration was scored 0 (no change or regular), 1 (1-30% necrotic cells), 2 (31-50% necrotic cells), and 3 (51-100% necrotic cells) (Solfaine et al. 2021).

Hematological Evaluation

The blood samples were collected into plain tubes and vacutainers for differential leucocyte analysis. All fresh blood samples in plain tubes were spun at 4000rpm for 15min (Hettich EBA, Germany). The whole blood was measured using the hematology analyzer Hitachi 902® (Roche, USA).

Statistical Analysis

Parametric data were tabulated as mean+SD and analyzed with ANOVA test (one-way analysis of variance) and Duncan's post hoc comparison test. Non parametric

data of histopathology were score as mean values was applied for Kruskal Wallis and Mann-Whitney tests with a confidence interval of 95% by SPSS 21.

RESULTS

According to the results of the hematological profile in differential leukocyte count, significant improvements ($P<0.05$) were found in leukocytes, lymphocytes, and neutrophils levels. A significant fluctuation ($P<0.05$) was found in the leukocyte, hemoglobin, and neutrophil variables of D3 compared to the D1 and D2 groups. The leukocyte and lymphocyte levels were significantly decrease ($P<0.05$) in D3 compared to the D1 group (Table 1). Meanwhile the hemoglobin value was increased in treatment group D3 compared with D1 and D2 groups. These results indicated that there was an improvement in the hematological profile after the administration of *Bdellovibrio bacteriovorus* isolate dose of 1mL/kg bw.

The score of duodenal histopathology in D3 (treatment group) which received Bb isolate showed significantly decreased ($P\leq0.05$) necrosis and cellular infiltration scores compared to D1 and D3. These scores were significantly different ($P\leq0.05$) between the treatment groups D2 and D3 (Table 2).

Histopathology cross-section of mice duodenum showing villous mucosa structure and crypts is presented in Fig. 1. Microscopic examination showed the presence of focal necrotic cells with vacuolization of enterocytes in the villous mucosa. Intestinal section indicated vacuolization and edema of villous mucosa accompanied by infiltration of histiocytes. The mucosal rupture was observed, resulting in the accumulation of cellular debris and leukocytes in the lumen of the crypt mucosa. Many enterocyte cell vacuoles and rupture of the villous mucosa were accompanied by the proliferation of intestinal glands. Hemorrhages and histiocytic infiltration were also observed in the mucosal crypts. The focal atrophy of the villi was accompanied by mild shrinkage, enterocytes were found to contain a few vacuoles, and there was mild necrosis in the villi with little proliferation of the crypt epithelium. The duodenum section showing edematous crypt epithelium with villous atrophy as well as shortening and multifocal vacuolation of villous enterocytes is shown in Fig. 1. Based on the analysis of the hematological profile, the D1 group exhibited a higher count than the control in the following variables of leukocyte, hemoglobin, lymphocyte, and neutrophil (Table 1). The level of blood differential also showed a significant difference in the D1 and D2 compared to the D3 group (Table 1).

Table 1: The differential leukocyte counts and hemoglobin in various groups

Parameters	Units	D0	D1	D2	D3
Total Leukocytes	$10^3/mm^3$	7.70±0.62a	8.03±0.51b	8.33±0.50b	7.90±0.54c
Hemoglobin	g/dL	11.80±0.72a	9.11±1.61b	9.40±0.64b	11.54±1.70c
Lymphocyte	%	51.23±1.30a	57.73±1.40c	52.10±2.30a	53.50±2.01b
Neutrophil	%	24.50±2.50a	22.50±1.00b	29.50±2.50c	24.50±2.50a

Values (mean+SD) bearing different alphabets in a row showed significant ($P<0.05$) difference. D0=control group, D1=SE-induced group, D2=SE-induced +tiamphenicol group, D3=SE-induced +Bb isolate group.

Table 2: Comparison of different histopathology scores of duodenum tissues in various groups

Groups	Infiltrating cells	Necrotic cells
D0 (n=4)	1.20±0.41a	1.50±0.55a
D1(n=4)	1.75±0.90b	2.00±0.74b
D2 (n=4)	1.80±0.86b	2.00±0.74b
D3 (n=4)	1.20±0.41a	1.50±0.54a

Values (mean+SD) bearing different alphabets in a column showed significant ($P<0.05$) difference. HE=hematoxylin-eosin, D0=control group, D1=SE-induced group, D2=SE-induced +tiamphenicol group., D3=SE-induced +Bb isolate group

DISCUSSION

According to recent studies, *Bdellovibrio bacteriovorus* HD100 showed the capacity to attack *Aggregatibacter actinomycetemcomitans*, a major contributor to periodontitis. Further investigation found that different bacterial species associated with periodontitis could be attacked by one or more of Bdellovibrio strains, even when the prey was a strict anaerobe. This is remarkable as BALOs are strict aerobes and require oxygen to complete the predator cycle, while their prey will die when exposed to oxygen for prolonged periods (Rendulic et al. 2004; Hobley et al. 2020).

Previously studies showed that administration of *Bdellovibrio bacteriovorus* increased the number of leukocytes and decreased the number of RBC and platelets in mice inoculated with *Pasteurella multocida* and had no effect on rat hematology (Pan et al. 2011; Sar et al. 2020). Furthermore, B bacteriovorus (Bb) as an intracellular bacterium, produces hydrolase enzymes, which digest host cell contents to provide nutrients for growth and nuclease enzymes, thus degrading the target bacterial DNA. The DNase enzyme secreted from B. bacteriovorus isolates Bd0934 and Bd3507 is a nuclease enzyme secreted during the life cycle of Bb predators (Bukowska-Faniband et al. 2020; Mazkour et al. 2020).

The duodenum histopathology data showed that there were alterations, including cellular infiltration and necrosis, as well as indications of toxicity or infection. Neutrophilia was observed, and leukocytosis, indicating the presence of inflammatory cells was significant, suggesting that mice had been exposed to infectious diseases or chemical induction. These results suggested that relative to the control, there were pathological changes in the D1, D2, and D3 treatment groups (Fig. 1). Previously studied administration of *Bdellovibrio bacteriovorus* did not show histopathological effects on colonic tissue but there was a slight increase in proinflammatory cytokines IL-1β, IL-4, IL-5, IL-6, IL-10, IL-13, CXCL-1, IFNγ, and TNF-alpha measured in the rat colon after inoculation. Administration of Bb bacteria does not produce adverse pathological effects and does not cause a substantial immune response in the gut and there is limited change in the health beneficial gut bacterial population (Shatzkes et al. 2017).

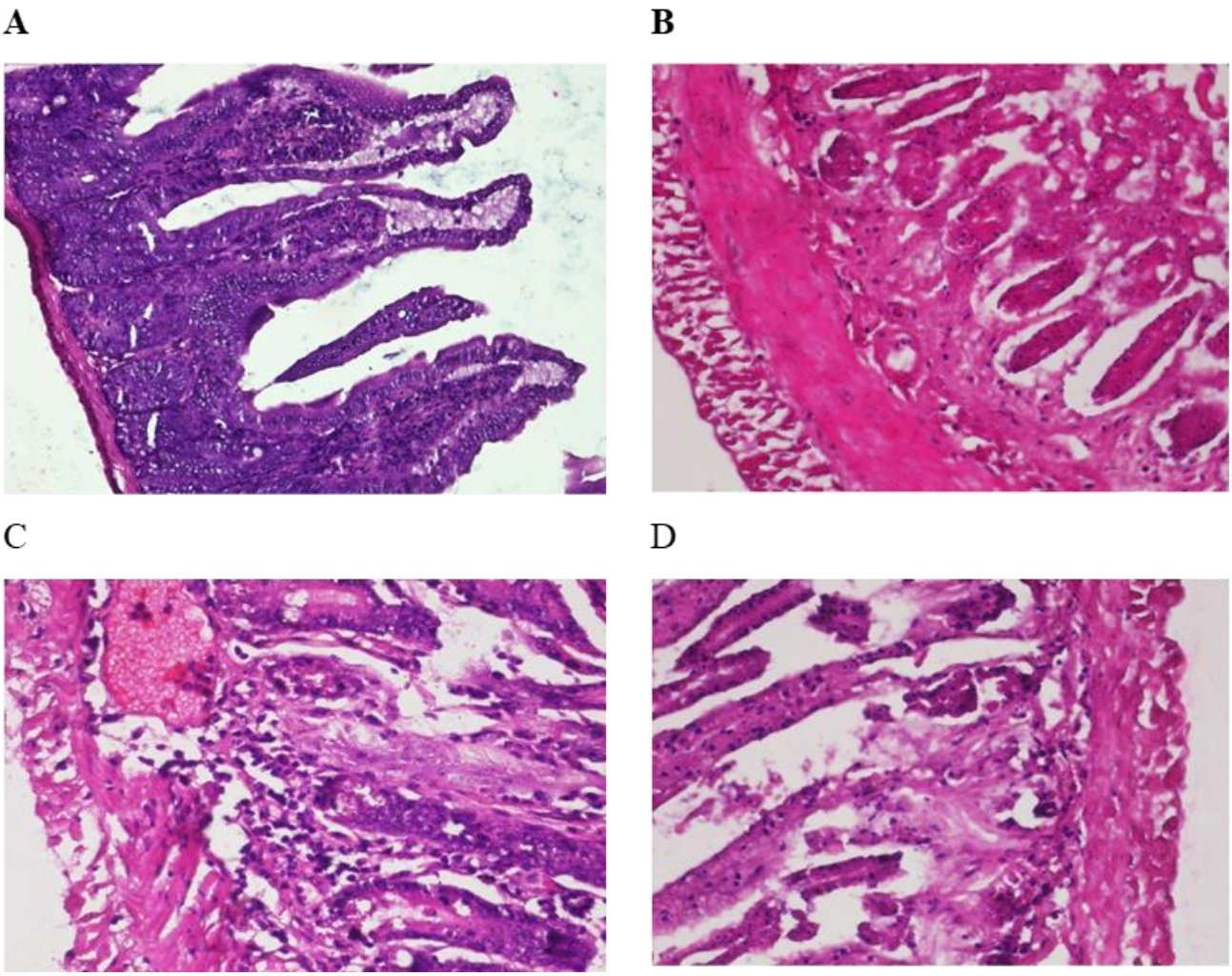

Fig. 1: Histomorphology section of the mouse duodenum showing normal villous mucosa structure and crypts (a), microscopic intestinal examination showing the presence of focal necrotic areas with vacuolation of enterocytes in the villous mucosa (b), edema of villous mucosa accompanied by infiltration of histiocytes (c), mucosal rupture with accumulation of cellular debris and leukocytes in the lumen of the crypt mucosa (d) (HE; 200x).

The results of this study showed a significant increase in neutrophils in the Bb treated group compared to the D1 group, which proved that Bb administration stimulated the phagocytosis process and did not suppress the immune system in white rats. Neutrophils are known to be able to phagocytize microorganisms and destroy them with bactericidal intracellular granules. In addition, neutrophils can capture and kill pathogens extracellularly with the same bactericidal mechanism through cytoneme networks and produce proteins forming neutrophil extracellular traps (NETs). In addition to antibacterial activity, cytonemes also function for cell adhesion and communication (Galkina et al. 2020).

The histological structure of the duodenum in the group treated with *Bdellovibrio bacteriovorus* showed mild level necrosis marked by intact intestinal villi and enterocyte cells complete if compared to the control group. Meanwhile, the structure of the villi was the most damaged in the D1 and D2 treatment groups which were characterized by rupture and desquamation of the epithelium followed by severe inflammation of the submucosa. The structural alteration in the histology of the duodenum due to feeding with isolate appeared to work without interfering with the normal functions. It is assumed that isolate can improve the characteristics of the natural microbes existing in the animal's body to restore the balance of the ratio between pathogenic and non-pathogenic bacteria in the digestive tract. Proteobacteria *Bdellovibrio bacteriovorus* is known to inhibit lung histopathological damage and there is an increase in the pro-inflammatory cytokine TNFα after *Klebsiella pneumoniae* inoculation in rats (Waso-Reyneke et al. 2022). *Bdellovibrio bacteriovorus* and other BALOs exhibit a relatively non-specific predatory behavior toward their host cells, attacking various gram-negative bacteria from very distinct and different genera. For example, the host range of *Bdellovibrio bacteriovorus* 109J encompasses strains from *Escherichia*, *Pseudomonas*, *Chromatium*, and *Spirillum* as well as pathogenic bacteria from numerous genera, including *Acinetobacter*, *Aeromonas*, *Bordetella*, *Burkholderia*, *Citrobacter*, *Enterobacter*, *Klebsiella*, *Listonella*, *Morganella*, *Proteus*, *Serratia*, *Salmonella*, *Shigella*, *Vibrio*, and *Yersinia*. The results showed that this strain could not attack *Campylobacter* (Schwudke et al. 2001; Snyder et al. 2002), while B bacteriovorus (Bb) strain, 100NCJB, showed potency against *Campylobacter jejuni*, and *Helicobacter pylori*. Inflammatory cell infiltration score showed that the

treatment group with *Bdellovibrio bacteriovorus* decreased significantly as evidenced by the low number of neutrophil cells in the mucosa and submucosa of the duodenum, while in the treatment group D1 and D2 there was increasing accumulation of inflammatory cells in the intestinal mucosa. This shows that administration of Bb can reduce inflammation by *S. enteriditis* inoculation.

These findings emphasize the versatility of various Bdellovibrio strains in preying upon a broad spectrum of pathogenic gram-negative bacteria affecting humans, animals, and plants (Roschanski and Strauch 2011; Mitchell et al. 2020). In a previous investigation, it was noted that *Pseudomonas aeruginosa*, a pathogen impacting individuals with cystic fibrosis and exhibiting reduced susceptibility to B. bacteriovorus 109 J, could potentially be targeted by another predatory bacterium, Micavibrio. Unlike Bdellovibrio, Micavibrio employs epibiotic processes and replicates through binary fission rather than septation. These results suggest the potential use of a combination of diverse predatory organisms to simultaneously combat multi-strain infections (Bonfiglio et al. 2020; Banks et al. 2022). Encouraging further research, a comprehensive investigation into the specific roles played by these isolates on vital organs and the identification of specific markers is essential. This in-depth exploration is aimed at reducing our reliance on antibiotics in the future, paving the way for innovative and targeted approaches to combat bacterial infection.

Conclusion

In conclusion, this study demonstrates that *Bdellovibrio bacteriovorus* (Bb) feeding exerts a notable impact on the dynamics of Salmonella enteritidis (SE) inoculation within the intestinal villi of mouse models. The experimental groups, particularly the SE+Bb inoculation (D3) group, displayed a significant increase in hematological parameters, including leukocytes, lymphocytes, and neutrophils. Notably, Bb feeding appeared to mitigate the destruction of epithelia and enterocytes in duodenal tissue, as evidenced by histomorphology analysis.

Acknowledgment

The authors are grateful to the Faculty of Veterinary Medicine, Universitas Airlangga Surabaya for supporting this study.

Authors contribution

ISH and RS were responsible for designing and conducting the study. RS, FF, and MTEP participated in sample collection and data analysis. The initial draft of the manuscript was written by ISH and RS, while FF, MTEP and STM revised it. All authors have reviewed and approved the final version of the manuscript.

REFERENCES

Banks EJ, Valdivia-Delgado M, Biboy J, Wilson A, Cadby IT, Vollmer W, Lambert C, Lovering AL and Sockett RE, 2022. Asymmetric peptidoglycan editing generates cell curvature in Bdellovibrio predatory bacteria. Nature Communications 13: 1509. https://doi.org/10.1038/s41467-022-29007-y

Bonfiglio G, Neroni B, Radocchia G, Marazzato M, Pantanella F and Schippa S, 2020. Insight into the possible use of the predator B bacteriovorus as a probiotic. Nutrients 12(8): 2252. https://doi.org/10.3390/nu12082252

Bratanis E, Andersson T, Lood R and Bukowska-Fanib and E, 2020. Biotechnological potential of Bdellovibrio and like organisms and their secreted enzymes. Frontiers in Microbiology 11: 662. https://doi.org/10.3389/fmicb.2020.00662

Bukowska-Faniband E, Andersson T and Lood R, 2020. Studies on Bd0934 and Bd3507, two secreted nucleases from Bdellovibrio bacteriovorus, reveal sequential release of nucleases during the predatory cycle. Journal of Bacteriology 202(18): E00150-20. https://doi.org/10.1128/JB.00150-20

Cavallo FM, Jordana L, Friedrich AW, Glasner C and van Dijl JM, 2021. Bdellovibrio bacteriovorus: a potential 'living antibiotic' to control bacterial pathogens. Critical Reviews in Microbiology 47(5): 630-646. https://doi.org/10.1080/1040841X.2021.1908956

Du XX, Gul ST, Ahmad L, Hussain R and Khan A, 2023. Fowl typhoid: Present scenario, diagnosis, prevention, and control measures. International Journal of Agriculture and Biosciences 12(3): 172-179. https://doi.org/10.47278/journal.ijab/2023.061

Galkina SI, Fedorova NV, Golenkina EA, Stadnichuk VI and Sud'ina GF, 2020. Cytonemes versus neutrophil extracellular traps in the fight of neutrophils with microbes. International Journal of Molecular Sciences 21: 586. https://doi.org/10.3390/ijms21020586

Herencias C, Salgado-Briegas S, Prieto MA and Nogales J, 2020. Providing new insights on the biphasic lifestyle of the predatory bacterium B bacteriovorus through genome-scale metabolic modeling. Public Library of Science Computational Biology 16(9): e1007646. https://doi.org/10.1371/journal.pcbi.1007646

Hobley L, Summers JK, Till R, Milner DS, Atterbury RJ, Stroud A, Capeness MJ, Gray S, Leidenroth A, Lambert C, Connerton I, Twycross J, Baker M, Tyson J, Kreft JU and Sockett RE, 2020. Dual predation by bacteriophage and B bacteriovorus can eradicate Escherichia coli prey in situations where single predation cannot. Journal of Bacteriology 202(6): e00629-19. https://doi.org/10.1128/JB.00629-19

Ibrahimi M, Loqman S, Jemo M, Hafidi M, Lemee L and Ouhdouch Y, 2023. The potential of facultative predatory Actinomycetota spp. and prospects in agricultural sustainability. Frontiers in Microbiology 13: 1081815. https://doi.org/10.3389/fmicb.2022.1081815

Im H, Dwidar M and Mitchell RJ, 2018. B bacteriovorus HD100, a predator of Gram-negative bacteria, benefits energetically from Staphylococcus aureus biofilms without predation. International Society for Microbial Ecology Journal 12(8): 2090-2095. https://doi.org/10.1038/s41396-018-0154-5.

Kaljević J, Saaki TNV, Govers SK, Remy O, van Raaphorst R, Lamot T and Laloux G, 2021. Chromosome choreography during the non-binary cell cycle of a predatory bacterium. Current Biology 31(17): 3707-3720.e5. https://doi.org/10.1016/j.cub.2021.06.024

Liu Y, Liu S, Pan Z, Ren Y, Jiang Y, Wang F, Li DD, Li YZ and Zhang Z, 2023. PAT: a comprehensive database of prokaryotic antimicrobial toxins. Nucleic Acids Research 51(D1): D452-D459. https://doi.org/10.1093/nar/gkac879

Lowry RC, Hallberg ZF, Till R, Simons TJ, Nottingham R, Want F, Sockett RE, Hammond MC and Lambert C, 2022. Production of 3',3'-cGAMP by a B bacteriovorus promiscuous GGDEF enzyme, Bd0367, regulates exit from prey by gliding motility. Public Library of Science Genetics 18(5): e1010164. https://doi.org/10.1371/journal.pgen.1010164

Mazkour S, Shekarforoush SS, Basiri S, Nazifi S, Yektaseresht A and Honarmand M, 2020. Effects of two probiotic spores of

Bacillus species on hematological, biochemical and inflammatory parameters in Salmonella Typhimurium infected rats. Scientific Reports 10(1): 8035. https://doi.org/10.1038/s41598-020-64559-3

Mitchell PS, Roncaioli JL, Turcotte EA, Goers L, Chavez RA, Lee AY, Lesser CF, Rauch I and Vance RE, 2020. NAIP-NLRC4-deficient mice are susceptible to shigellosis. Elife 9: e59022. https://doi.org/10.7554/eLife.59022

Mu DS, Wang S, Liang QY, Du ZZ, Tian R, Ouyang Y, Wang XP, Zhou A, Gong Y, Chen GJ, Van Nostrand J, Yang Y, Zhou J and Du ZJ, 2020. Bradymonabacteria, a novel bacterial predator group with versatile survival strategies in saline environments. Microbiome 8: 126. https://doi.org/10.1186/s40168-020-00902-0

Negus D, Moore C, Baker M, Raghunathan D, Tyson J and Sockett RE, 2017. Predator versus pathogen: how does predatory B bacteriovorus interface with the challenges of killing Gram-negative pathogens in a host setting? Annual Review of Microbiology 71: 441-457. https://doi.org/10.1146/annurev-micro-090816-093618

Odooli S, Roghanian R, Emtiazi G, Mohkam M and Ghasemi Y, 2020. Characterization of the first highly predatory B bacteriovorus from Iran and its potential lytic activity against principal pathogenic Enterobacteriaceae. Iranian Journal of Basic Medical Sciences 23(10): 1275-1285. https://doi.org/10.22038/ijbms.2020.43159.10146

Pan A, Chanda I and Chakrabarti J, 2011. Analysis of the genome and proteome composition of Bdellovibrio bacteriovorus: Indication for recent prey-derived horizontal gene transfer. Genomics 98: 213-222. https://doi.org/10.1016/j.ygeno.2011.05.008

Rendulic S, Jagtap P, Rosinus A, Eppinger M, Baar C, Lanz C, Keller H, Lambert C, Evans KJ, Goesmann A, Meyer F, Sockett RE and Schuster SC, 2004. A predator unmasked: life cycle of B bacteriovorus from a genomic perspective. Science 303: 689-692. https://doi.org/10.1126/science.1093027

Roschanski N and Strauch E, 2011. Assessment of the mobilizable vector plasmids pSUP202 and pSUP404.2 as genetic tools for the predatory bacterium Bdellovibrio bacteriovorus. Current Microbiology 62: 589-596. https://doi.org/10.1007/s00284-010-9765-9

Sar TT, Umeh UE and Amali O, 2020. Haematological evaluation of Sprague-Dawley rats infected with Pasteurella multocida and administered B bacteriovorus (ATCC™ 1534) as therapy. Open Journal of Bioscience Research 1(1): 1-8. https://doi.org/10.2734-2069

Schwudke D, Strauch E, Krueger M and Appel B, 2001. Taxonomic studies of predatory Bdellovibrios based on 16S rRNA analysis, ribotyping and the hit locus and characterization of isolates from the gut of animals. Systematic and Applied Microbiology 24: 385-394. https://doi.org/10.1078/0723-2020-00052

Shatzkes K, Tang C, Singleton E, Shukla S, Zuena M, Gupta S, Dharani S, Rinaggio J, Connell ND and Kadouri DE, 2017. Effect of predatory bacteria on the gut bacterial microbiota in rats. Scientific Reports 7: 43483. https://doi.org/10.1038/srep43483

Waso-Reyneke M, Khan S and Khan W, 2022. Interaction of B bacteriovorus with Gram-negative and Gram-positive bacteria in dual species and polymicrobial communities. Microorganisms 10: 793. https://doi.org/10.3390/microorganisms10040793

Snyder AR, Williams HN, Baer ML, Walker KE and Stine OC, 2002. 16S rDNA sequence analysis of environmental Bdellovibrio-and-like organisms (BALO) reveals extensive diversity. International Journal of Systematic and Evolutionary Microbiology 52: 2089-2094. https://doi.org/10.1099/00207713-52-6-2089

Solfaine R, Muniroh L, Sadarman, Apriza and Irawan A, 2021. Roles of Averrhoa bilimbi extract in increasing serum nitric oxide concentration and vascular dilatation of ethanol-induced hypertensive rats. Preventive Nutrition and Food Science 26(2): 186-191. https://doi.org/10.3746/pnf.2021.26.2.186

Youdkes D, Helman Y, Burdman S, Matan O and Jurkevitch E, 2020. Potential control of potato soft rot disease by the obligate predators Bdellovibrio and like organisms. Applied and Environmental Microbiology 86(6): e02543-19. https://doi.org/10.1128/AEM.02543-19