Effect Of Non-Protein Amino Acid (BABA) On Gastrointestinal Tissues Of Male Rats And Some Negative Enterobacteria.

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Abstract

The study was conducted to evaluate the effect of beta-aminobutyric acid (BABA) on negative intestinal bacteria and gastrointestinal tissues (stomach, small intestine and large intestine) of male rats. The rats were dosed with BABA orally four times a week. The results showed that the histological structure of the digestive system of the control treatment was normal. Also, the histological structure of the stomach was normal for all concentrations of acid. As for the small intestine and large intestine, its histological structure was affected with the increase in concentration. As for the studied negative enterococcus bacteria, it was also affected by the addition of (BABA), it decreased with increasing concentration.

Key words: β-aminobutyric acid, microbes, tissues, digestive system.

INTRODUCTION

The stomach is the most important part of the digestive system. The most complex endocrine organs with physiology, biochemistry, immunology, and microbiology. It is also the first line of defense against foodborne microbes. It may be affected physiologically when infected with a chronic bacterial infection that causes most peptic ulcer diseases and stomach cancer (Hunt et al, 2015). The small intestine is an abdominal tubular structure that absorbs important nutrients. Likewise, the large intestine is a tube consisting of several sections. The small intestine is connected to the large intestine, via the ileal valve. It is a physiological sphincter that reduces reflux into the small intestine (Freeman, 2006)

The microbial community that inhabits the host gut is associated with several physiological functions (Geva-Zatorsky et al, 2017; Gould et al, 2018).

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There is an association between intestinal microbiota, bowel disease, cancer, and obesity (Xu et al, 2017; Ma et al, 2018). There is also an association between the gut microbiota and cardiovascular disease, chronic disease (Ipci et al, 2017; Ruiz-Rodriguez & Rello, 2017; Shivaji, 2017; Blutt et al, 2018; Davidson & Epperson, 2018). Gut bacteria may lead to metabolic disease (Rivera-Piza & Lee, 2020).

Amino acids are the building blocks of proteins, and may contribute to improve cell function in T2DM mice (Ayon, 2020; Tan et al, 2021). Its introduction into peptides can enhance biological activities, improve membrane permeability and drug encapsulation, and may play an effective role in protecting neuron-like cells so it is considered a pharmacological agent for the treatment of neurological diseases, but also account for undesirable effects such as toxicity or immunogenicity (Song et al, 2021; Arokianathan et al, 2020; Minato et al, 2022; Ding et al, 2020). (Song et al, 2021; Arokianathan et al, 2020; Minato et al, 2022; Ding et al, 2020)

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Beta-aminobutyric acid (BABA) was shown to reduce insulin resistance in skeletal muscle, modulate the defense system at the molecular level, non-allergy producer, improve antioxidant capacity, and have anti-diabetic activities (Sawada et al, 2019; Choudhary et al., 2021; Sagheer & Jasim, 2020; Selim et al., 2022; Mahmud et al., 2022; Quan et al, 2022). Low concentrations of (BABA) did not affect the tissues of male rats (Saleh & Jasim, 2018). Amino acids such as BABA can help fight many diseases and have the ability to reduce liver tissue damage in diabetic mice (Tao et al., 2022; Yao et al., 2020; Thamer and Jasim, 2021). No signs of toxicity were seen when rats were dosed with GABA at doses of up to 1 g/kg (Oketch-Rabah et al, 2021).

Non-proteinogenic amino acids (NPAAs) have attracted great interest for their fundamental applications in biology and chemistry (Yuan et al, 2020). It can be involved in the food chain. Some are toxic through their ability to mimic the amino acids of the protein (Samardzic et al, 2019). Some of them are implicated in the induction of neurodegenerative diseases and Alzheimer's disease, are water soluble, and can bioaccumulate in the food chain (Dunlop & Guillemin, 2019). Amino acids not only act as regulatory molecules, Furthermore, they can be included in catabolism or have toxic effects (Hener et al, 2018). It has also been shown to be neurotoxic as BMAA and may play an important role as an environmental factor in disease onset (Main, 2018).

Transport of amino acids through enterocytes in the intestinal mucosa is complicated by their entry into either the anabolic or catabolic pathways, thus reducing their availability (Macillline et al, 2021). It has the ability to increase resistance against organisms, thereby inhibiting it and limiting its spread (Li et al, 2021). It was also found that BABA has the ability to resist bacteria (Al-Ta'i, 2021). Compounds containing non-proteinogenic amino acids show high antimicrobial activity (Yokoo et al, 2021). It may stimulate immune responses resulting in long-lasting resistance (Hegedos et al, 2022). D-amino acids may also have a number of toxic effects and should be added at low levels (Grishin et al, 2020).

MATERIAL AND WORKING METHODS

Experience Design

Male rats were used with ages ranging from 10-12 weeks, weights varied between (210-160) grams, suitable environmental conditions were created for them, and they underwent a period of acclimatization for 10 days before starting the experiment. Rats were divided into four groups, each group had five animals, and dosed at four levels: 100, 200, 300 g/kg and the control treatment (without addition) A, B, and C, respectively, and the animals dosed at four stages (T1 = the first dosing stage, T2 = second dosing stage, T3 = third dosing stage and T4 = fourth dosing stage.

Processing of beta-aminobutyric acid

Prepared by dissolving it in 10 ml of distilled water, according to the concentration assigned to each group, then preparing the required doses according to the weight of the animal and the dose of the animals every seven days for four weeks. Using a dosing gavage (Perret-Gentil, 2010).

Collection of models

Samples were taken from the waste of male rats before starting the dose and after each stage of dosing, then transferred to the laboratory for the necessary procedure.

Bacterial isolation and identification

Characterization of bacterial isolates by culturing them on Mac Conkey agar medium and Nutrient agar medium and then performing phenotypic and biochemical assays.

Phenotypical bacterial tests

Bacterial tests were performed morphologically and microscopically (MacFadden, 2000).

Biochemical bacterial tests

Several tests were carried out on bacterial colonies isolated from rat excreta after the dilution procedure, and the studied bacterial isolates were confirmed using the VITEK®2 device (MacFadden, 2000).

Identification of Tissue Sections

Organs were preserved in 10% formalin solution. The tissues were taken out of the solution, then cut and placed in special capsules, then placed in a device containing eight cylinders. The first five cylinders contain ethyl alcohol at sequential levels starting from 50%, 70%, 90%, 100%, 100%. The sixth cylinder contained xylene, while the seventh and eighth cylinders contained paraffin with a melting point of 60 ° C. The samples remain in the cylinders for a specified period of time (Drury, Allington & Cameron, 1967).

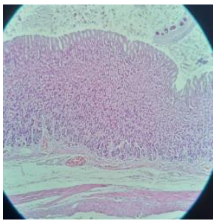
The samples are placed in molds and then wax with a melting point of 80 ° C is poured over the samples and left to solidify. Excess wax was removed with a special device. To facilitate the cutting process, the molds are heated to 20 ° C. 4 μm thick sections were cut, surfaced in a 45°C water bath, and loaded onto glass slides after coating them with glycerol and egg white in order to increase adhesion.

RESULTS AND DISCUSSION

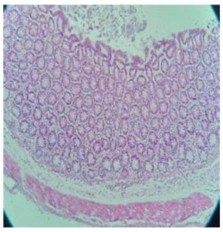
Effect of β-aminobutyric acid (BABA) on gastrointestinal tissues of male rats

1- Stomach

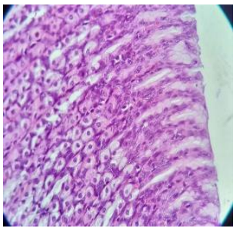
The results of the examination of histological sections (Figure 1) showed that the geometric structure of the stomach tissues was normal and there were no changes in both the control group (without adding acid), the first concentration group A (100 mg / kg) and the second concentration B (200 mg / kg). kg) of dosing with amino acid, as well as the third concentration group (300 mg / kg), despite the increase in concentration, but the examination of histological structure showed that the layers of stomach tissue appeared normally, and this indicates that dosing with β-amino butyric acid (BABA) did not affects the histological structure of stomachs of male rats used in the experiment. This is what Al-Kubaisi, (2020) found in his study that adding BABA at certain concentrations did not affect the geometric structure of stomach tissues. It also agrees with (Chen et al, 2021), as they found that GABA led to an increase in body weight with a specific rate of growth, and an increase in the efficiency of nutrition and protein. The results were consistent with results (Tang & Chen, 2016), which showed that γ-aminobutyric acid improved immune function, development and tissue integrity. It also agreed with the results (Al-Karishi et al., 2021) that GABA-A acid represents a new treatment method for patients with type 1 and type 2 diabetes, and it also works to improve pancreatic cell function and insulin sensitivity by activating GABA-A receptors. In line with the results (Aktas & Gur, 2021a,b), the histological structure of the hippocampus, cortex and cerebellum in diabetic mice was normal and no pathological changes were detected in the central nervous system. (Aktas & Gur, 2021b) found that BAIBA preserved histological and biochemical changes in serum and kidneys of rats. Also (Tamai et al, 2020) that a compound containing non-proteinogenic amino acids attenuates liver damage in mice.



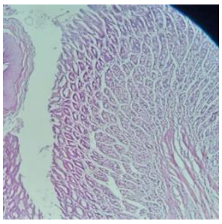
Focus Group I (A)



control group (D)



Focus group III (C)

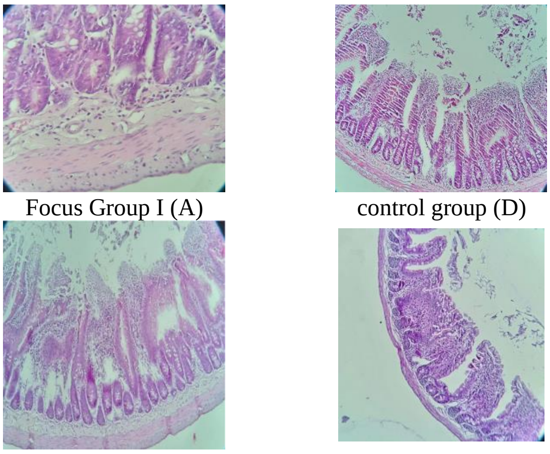


Second focus group (B)

Figures 1. Shows histological sections of the small intestine of male rats, stained with H&E (Haematoxylin and Eosin) stain.

2. Small intestine

It was found through histological examination of the small intestine (Figure 2) that beta-amino-butyric acid (BABA) had a clear effect on the geometrical structure of small intestine tissues at all concentrations, but in varying proportions according to the increase in concentration compared to the control group D (without addition) in which the geometric structure appeared For the small intestine normally, concentration group A (100 mg/kg) showed infiltration of inflammatory cells with shedding of endothelial cells, and focus group B (200 mg/kg) showed an overabundance of goblet cells and shedding of endothelial cells with inflammation in the cells. Focus group C (300 mg/kg) Acute inflammation with villous union and adhesion. The reason may be attributed to the nature of the function of the small intestine through its high absorptive capacity, in which nutrients are digested and absorbed. It agrees with (Barido et al, 2021) that high doses of GABA may lead to a significant impairment in the performance of the animal and its tissues. This is also consistent with (Bouchebti et al, 2022) as it was found that an increase in the concentration of BABA can negatively affects body tissues.



Focus Group I (A) control group (D)

Focus group III (C) Second focus group (B)

Figures 2. Of histological sections of stomach of male rats. H&E (Haematoxylin and Eosin) dyed dye.

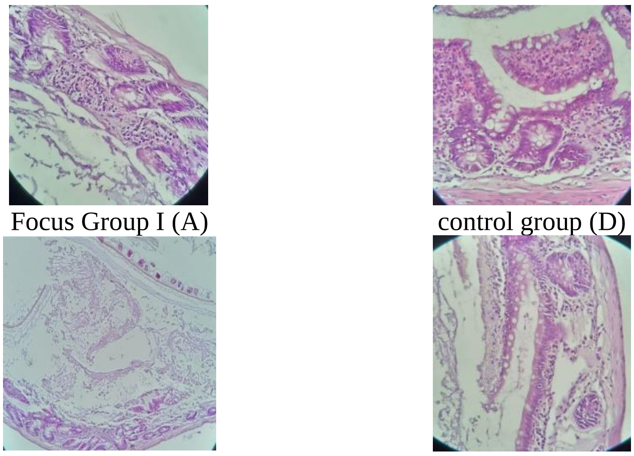
3. Large Intestine

The results of the histological examination of the large intestine (Figure 3) showed that the amino acid (BABA) had an effective role in influencing the geometric structure of the large intestine tissues in the different concentrations used in the study, but in varying proportions according to the increase in concentration, as it was found that the first concentration (100 mg / kg) did not significantly affect the engineering structure of the large intestine despite the presence of a slight inflammation in the endothelial cells, while the second concentration (200 mg / kg) of homocysteine caused the infiltration of inflammatory cells into the mucosa with hyperproliferation of endothelial cells and the concentration also led The third (300 mg/kg) leads to an increase in the infiltration of inflammatory cells within the mucosa and submucosa with hyperproliferation of endothelial cells. It also agrees with (Barido et al, 2021), who indicated in his study about the effect of a diet supplemented with beta-aminobutyric acids, High doses of GABA may lead to a significant imbalance in the performance of the animal and its tissues. This is consistent with (Bouchebti et al, 2022) as it was found that an increase in the concentration of non-proteinogenic amino acid can negatively affect body tissues.

EFFECT OF BABA ON SOME ENTERO-NEGATIVE BACTERIA

1. *E. coli*

The results of the current study (Fig. 1) showed that animal dosing with amino acids had an effective effect on bacteria, as the third level (C) gave the lowest rate of the number of bacterial colonies, but rather the disappearance of bacteria, especially in the third and fourth dosing stages compared to the control treatment that achieved higher Average isolates reached 87 isolates. It was also found that the stages of dosing have an effective role in influencing E. coli and thus led to a reduction in the number of isolates and even their disappearance, especially in the last stages of dosing compared to the control treatment. This shows the importance of the animals being dosed in batches, which had a significant impact on the number and type of bacteria. These results agree with (Gur, Reuveni & Cohen, 2021) which showed that BABA showed resistance against microorganisms. It also agrees with (Al-Taei, Jassem and Zughayer, 2021; Bellamici et al., 2021) that BABA can act as an antibacterial. This is what (Jafarbeigi, Samih & Alaei, 2021) found that compounds containing BABA have the ability to regulate defensive responses to resist biotic and abiotic stresses.



Focus Group I (A) control group (D)

Focus group III (C) Second focus group (B)

Figures 3. Shows histological sections of the large intestine of male rats. H&E (Haematoxylin and Eosin) dyed.

2. Klebsiella Pneumoniae

The results (Fig. 2) showed that BABA had a significant effect on *K. pneumoniae* bacteria, as the third level (C) gave the lowest average number of bacterial colonies, followed by the second level and the first level, in order. Compared with the control treatment, which gave the highest rate of the number of bacterial colonies, it was 72 isolates. The stages of dosing effectively affected the bacteria, if the third and fourth stages of dosing gave the lowest rate of bacterial colonies. It also led to the disappearance of bacteria in high levels of acid. It is clear from the above the ability of the amino acid to increase the resistance of animals and strengthen their immune system and thus reduce the proliferation of bacteria. It also agrees with what was mentioned (Yu et al, 2022) that treatment with non-proteinogenic amino acid (BABA) led to a reduction in the proliferation of living organisms, as well as with (Khlaif et al, 2020), as it was found that β-aminobutyric acid (BABA) can act as an anti-bacterial .

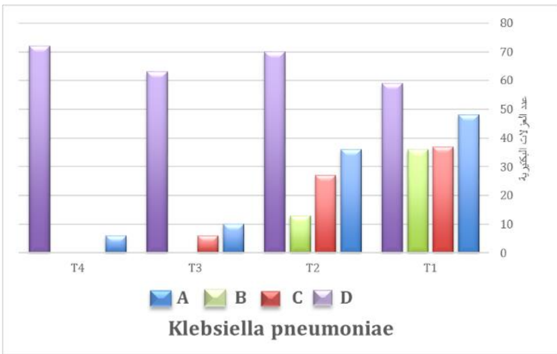


Figure 1. Effect of Beta-aminobutyric acid (BABA) on *E. coli*.

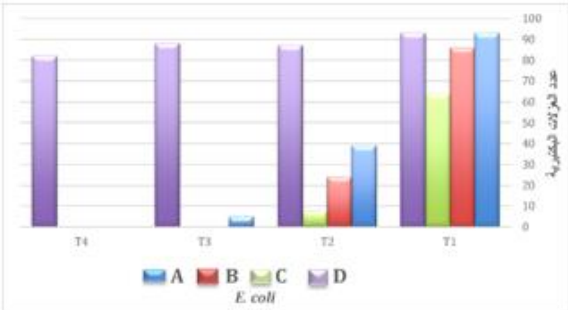


Figure 1. Effect of Beta-aminobutyric acid (BABA) on *Klebsiella pneumonia*.

3. Brucella Melitensis

It was found through the results that β-aminobutyric acid (BABA) led to the inhibition and disappearance of bacteria, especially the third concentration (C) for all stages of dosing, Followed by the second concentrations (B) and the first (A) in order, compared to the control treatment, which achieved the highest average number of bacterial colonies of 43 bacterial isolates (Fig. 3). The dosing stages also had an effective role in influencing the number of bacterial isolates, as the fourth (T4) and third (T3) dosing stages reduced the disappearance of bacteria for different concentrations, followed by the second dosing stage. a. The results are in agreement with (Asif et al, 2021) as it was found that BABA effectively affected the proliferation of microbes. It also agrees with his findings (Chalupowicz et al, 2021) that BABA inhibits bacterial multiplication. The results also agree with what was mentioned (Farris et al, 2022) that the addition of GABA improved the resistance against endogenous streptococcal infection. It is consistent with what was found (Ansari et al, 2019) that the addition of BABA led to a decrease in the number of bacteria. It also agrees with (Ikeda et al, 2021) as it was revealed that non-protein amino acids show an inhibitory activity of bacterial biofilms, which leads to their inhibition.

CONCLUSIONS

The results showed that the histological structure of the stomach was not affected by the addition of B-amino butyric acid, and the tissues appeared normally, while it clearly affected the tissues of the small intestine, and also led to the emergence of acute inflammation with associated and villous adhesion. The large intestine was also affected by the addition of BABA, which resulted in increased infiltration of inflammatory cells with excessive proliferation of endothelial cells. The results showed that the negative enteric bacteria (*E. coli, K. pneumonia, B. melitensis*) decreased significantly and even disappeared with increasing concentration.

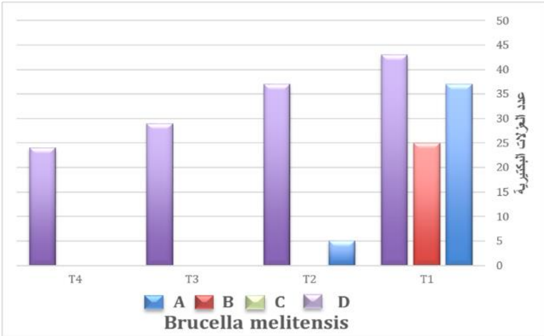


Figure 3. Effect of Beta-aminobutyric acid (BABA) on *Brucella melitensis.*

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