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Git Microbiome: The Effect of Finger Millet (*Eleusinecoracana*) Seed Extract on Albino Wistar Rats

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Abstract:- The objective of this study is determine the effect of *Eleusinecoracana* seed extract on gastrointestinal tract (GIT) microbiome of Wistar rat induced with tramadol. Twenty (20) healthy Wistar albino rats were weighed and allowed to acclimatize for one week with free access to food pallets and water and libitum. They were grouped into three (3) groups of four (4) rats each as group T1, T2 and control. Group T1 and T2 were administered with 0.1 and 0.2 g of the ethanolic extract respectively, while control were given distilled water. The study shows an increase in the weight of Wistar rat administered with high dosage of the plant extract when compared to those administered with low dosage of the extract and also the control group. Different microbial isolates isolated from the fecal and GIT of Wistar rats include; *Aeromonashydrophyla*, *Proteus* spp., *Pseudomonasaeruginosa*, *Citrobacterfreundii*, *S.* spp., *Staphylococcusaureus*, *C. freundii*, and *Providencia* spp. The study revealed that the negative control group contains *Pseudomonas aeruginosa* with percentage incidence of 28.1%, followed by *A. hydrophyla* and *Proteus* spp., with percentage incidence of 25 and 21.9% respectively, while *Citrobacterfreundii* has the lowest percentage incidence of 3.1%. While positive group and group administered with the plant extract had *Providencias*pp as the only organisms present with percentage incidence of 100%.From the study, it was revealed that the extract of finger millet have effect on the microbiome of the GIT with a reduction in the population of bacteria colonies. The population of the bacterial colonies were reduced drastically on administration of the plant extract and tramadol.

Keywords:- *Gastrointestinal tract, colony count, finger millet, antimicrobial.*

I. INTRODUCTION

The gut is a complex and dynamic network in which the host and gut microbes interact to form a balanced, symbiotic, and mutually beneficial connection (Kau*et al*., 2011). The state of resilience and resistance to exogenous and endogenous disruptions is referred to as gut homeostasis (Lozupone*et al*., 2012). The commensal bacteria, a functional barrier, and a tolerant immune response all contribute to gut homeostasis (Brown *et al*., 2013). All microorganisms found in the gastrointestinal (GI) tract, including bacteria, archaea, eukaryotes, fungi, and viruses, are considered part of the gut microbiota (Gordon, 2012). The term "microbiome" refers to an environment's whole collection of microbial genes (The Human Microbiome Project Consortium, 2012).

Microbial dysbiosis is defined as a change in the structural and/or functional configuration of the gut microbiota that disrupts gut homeostasis and is linked to obesity, diabetes, autoimmune diseases, neurological disorders, allergies, inflammatory diseases as well as infectious diseases (Gordon, 2012; Sommer and Bäckhed, 2013). In humans and mice, changes in the microbiota's composition or density have been demonstrated to enhance vulnerability to infections and aberrant mucosal immune responses (Stecher and Hardt, 2008; Wells *et al*., 2011). Antibiotic-induced changes in the gut microbiome and metabolome of mice, for example, increase susceptibility to Clostridium difficile infections (Theriot*et al*., 2014).

Natural remedies have been utilized to improve health since the beginning of humanity, and current medical science relies heavily on pharmaceuticals derived from natural resources. For the treatment and control of infectious agents, a vast number of antimicrobial compounds were developed from synthetic and natural sources (Shriram*et al*., 2018). Only a few of these, however, were accessible to the world's hungry market (Poulakou*et al*., 2018). The rise of multidrug-resistant bacteria has posed a new threat to the availability and price of many antibiotics now prescribed around the world (Falcone and Paterson, 2016; van Duin and Doi, 2017).

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Eleusinecoracana, commonly known as African finger millet, is a cereal produced in desert areas of Africa and Asia. Tamba is the Hausa word for it, and oka is the Yoruba word for it. It's a storehouse of phytochemicals, minerals, anti-nutrients, and key proximate metabolites (Chethan and Melleshi, 2007). The millet could be consumed raw, cooked, or processed in other ways, such as milling, boiling, and roasting, as is common in Nigeria. It can be kept alive for many years without treatment or infestation by insects or pests, making it an excellent reserve food (Japhet*et al*., 2018).The main objective of this study is determine the effect of *Eleusinecoracana* seed extract on gastrointestinal tract (GIT) microbiome of Wistar rat induced with tramadol.

II. MATERIALS AND METHODS

A. *Collection and Identification of Finger Millet (Eleusinecoracana) Seed*

The sclerotia of *Eleusinecoracana* were bought from Jos plateau State at Jos ultra-modern market (Also known as terminal market), east-central Nigeria. The ethanol extract of the millet was prepared from the powdered sample of the millet. Three hundred gram (300g) of the powdered millet was soaked into 1400ml of absolute ethanol for 5days. The extract was then filtered with muslin cloth and concentrated by evaporating excess solvent in a hot water-bath. The resulting concentrate was then reconstituted using distilled water for a final weight per volume of 100mg/ml, and stored in a refrigerator at 4°C until when it was required for use in the experiment. The weights of the ethanol extract (yield) was 5.9g which gave percentage yield of 1.97%. The percentage yield were calculated using the formula below:

B. *Experimental Animals*

Twenty (20) healthy Wistar albino rats were purchased from the animal house of the Department of Pharmacology, Delta State University, Abraka and maintained at room temperature under 12hour dark cycle for one week to acclimatize. The animals were weighed and allowed to acclimatize for one week with free access to food pallets and water and libitum. The Wistar albino rats were randomized into three (3) groups of four (4) rats each as group T1, T2 and control. The four rats in group T1 were administered with 0.1 g of the ethanolic extract, while group T2 were administered with 0.2g of the ethanolic extract while control were given distilled water. All treatments were administered via oral route with the aid of a cannula for fourteen (14) days.

a) Animal Monitoring

The animal were administered with the millet extracts once daily. The fecal of the rats from each group was collected on day 0 and day 14 and then cultured in a broth medium in an incubator at 37°C for 24hours. On day 14, the animals were then sacrificed and processed for different biochemical parameters. The gastrointestinal tracts of the sacrificed animals from each group was excised and the internal section swabbed and cultured in a broth medium in an incubator at 37°C for 24hours, and bacterial growth observed, colonies identified and counted to determine the microbial load. Body weights were also recorded on days 0 and 14.

C. *Sterilization of Materials*

Glass wares such as text-tubes, beakers, glass rods, measuring cylinders, Durham's tubes, droppers, McCartney's bottles, forceps, and Agar bottles were washed with detergents and rinsed under running tap after they were sterilized in an autoclave at 121°C for 25minutes. All culture media were also sterilized in an autoclave at 121°C for 15minutes except the Urea broth that was sterilized by filtration using a sterile Whatman's filter paper. The wire loop was sterilized by flaming while the glass spreader was sterilized with alcohol and flame.

D. *Preparation of Media*

Bacterial media used were prepared according to manufacturer's instruction and labelled accurately.

III. RESULTS

Treatment Days	Groups		
	T1	**T2**	**Control**
0	105.5±2.41	105.25±6.61	94.25±2.04
7	129.00±2.00	131.5±3.13	97.5±2.05
14	129.25±2.64	132.5±2.86	101.75±4.31

Table 1: Weight of Wistar rats before and after administration of *Eleusinecoracana* plant extract

mean±SEM values of weight of Wistar rats (n = 4); T1 = group of Wistar rats administered with 0.1g of plant extract; T2 = group of Wistar rat administered with 0.2g of plant extract and tramadol; Control = group administered with only water

	Colony count		
	T1	**T2**	**Control**
R1	TNTC	TNTC	TNTC
R2	TNTC	TNTC	TNTC
R3	TNTC	TNTC	TNTC
R4	TNTC	TNTC	TNTC

Table 2: Colony Count before Administration of *Eleusinecoracana* Plant Extract

TNTC: Too numerous to count

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	Number of Colony					
	T1		T2		Control	
	Fecal	GIT	Fecal	GIT	Fecal	GIT
R1	360	356	419	400	450	TNTC
R2	370	247	470	450	480	TNTC
R3	393	370	478	430	TNTC	TNTC
R4	390	359	247	200	390	TNTC

Table 3: Colony Count after Administration of *Eleusinecoracana* Plant Extract

Key:
R1 – R4: Code for Wistar rats
TNTC: Too numerous to count

Code for the bacteria Identified	Catalase	Indole	H_2S	MR-VP	Simon Citrate	Motility	Oxidase	Urease	MIU confirmation	Gram-staining	Coagulase	Fermentation			Name of suspected organisms
												S	G	L	
Nutrient agar															
1	+	+	+	+	+	+	+	-	+	+	+	A	A	A	Aeromonas
2	+	+	+	+	+	+	+	+	+	+	+	A	A	A	Proteus spp
3	+	+	+	+	+	+	+	+	-	+	+	A	A	A	Proteus spp
4	+	+	+	+	+	+	+	-	+	-	-	A	A	A	Aeromonas
5	+	+	+	+	+	+	+	-	+	-	-	A	A	A	Aeromonas
6	+	+	+	+	+	+	+	-	+	-	-	A	A	A	Aeromonas
7	+	+	+	+	+	+	+	+	+	+	+	A	A	A	Proteus spp
8	+	+	+	+	+	+	+	+	+	+	+	A	A	A	Proteus spp
Centrimide															
1	+	-	-	-	+	+	+	-	-	-	-	-	A	-	Pseudomonas
2	+	-	-	-	+	+	+	-	-	-	-	-	A	-	Pseudomonas
3	+	-		-	+	+	+	-	-	-	-	-	A	-	Pseudomonas
4	+	-	-	-	+	+	+	-	-	-	-	-	A	-	Pseudomonas
5	+	-	-	-	+	+	+	-	+	-	-	-	A	-	Pseudomonas
6	+	-	-	-	+	+	+	-	-	-	-	-	A	-	Pseudomonas
7	+	-	-	-	+	+	+	-	+	-	-	-	A	-	Pseudomonas
8	+	-	-	-	+	+	+	-	-	-	-	-	A	-	Pseudomonas

Table 4a: Biochemical Test Result for Microorganisms isolated from the Wistar rats before the Administration of *Eleusinecoracana* Plant Extract (Negative control)

(+) stands for positive result, (-) stands for negative result, A; acid and gas

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Code for the bacteria Identified	Catalase	Indole	H_2S	MR-VP	Simon Citrate	Motility	Oxidase	Urease	MIU confirmation	Gram-staining	Coagulase	Fermentation			Name of suspected organisms
												S	G	L	
Mc-Conkey Agar															
1	+	+	+	+	+	+	+	-	+	-	-	A	A	A	Proteus spp
2A	+	+	+	+	+	+	+	+	+	-	-	A	A	A	Proteus spp
2B	+	-	+	+	+	+	+	-	-	-	-	-	A	-	Citrobacter
3	+	+	+	+	+	+	+	-	-	-	-	A	A	A	Aeromonas
4	+	-	-	-	+	+	+	-	+	-	-	-	A	-	Pseudomonas
5	+	+	+	+	+	+	+	+	-	-	-	A	A	A	Aeromonas
6	+	+	+	+	+	+	+	+	+	-	-	A	A	A	Proteus spp
7	+	+	+	+	+	+	-	-	-	-	-	A	A	A	Aeromonas
8	+	+	+	+	+	+	-	-	-	-	-	A	A	A	Aeromonas
Mannitol Salt Agar															
1	+	-	-	-	-	-	-	-	+	+	-	A	A	A	S. spp
2	+	-	-	-	-	-	-	+	+	+	+	A	A	A	S. aureus
3	+	-	-	-	-	-	-	+	+	+	+	A	A	A	S. aureus
4	+	-	-	-	-	-	-	+	+	+	-	A	A	A	S. spp
5	+	-	-	-	-	-	-	+	+	+	-	A	A	A	S. spp
6	+	-	-	-	-	-	-	+	+	+	-	A	A	A	S. spp
7	+	-	-	-	-	-	-	+	+	+	+	A	A	A	S. aureus
8	+	-	-	-	-	-	-	+	+	+	+	A	A	A	S. aureus

Table 4b: Biochemical Test Result for Microorganisms isolated from the Wistar rats before the Administration of *Eleusinecoracana* Plant Extract (Negative Control)

(+) stands for positive result, (-) stands for negative result, A; acid and gas

Code for the bacteria Identified	Catalase	Indole	H_2S	MR-VP	Simon Citrate	Motility (MIU)	Oxidase	Urease	MIU (Urease)	Gram-staining	Coagulase	Fermentation			Name of suspected organisms
												S	G	L	
Extract															
TL 1A	+	+	-	+	+	+	-	-	-	-	-	A/G	A/G	A/G	Providencia
TL 1B	+	+	-	+	+	+	-	+	-	-	-	A/G	A/G	A/G	Providencia
TL 2	+	+	-	+	+	+	-	+	+	-	-	A/G	A/G	A/G	Providencia
TL 3A	+	+	-	+	+	+	-	-	-	-	-	A/G	A/G	A/G	Providencia
TL 3B	+	+	-	+	+	+	-	+	+	-	-	A/G	A/G	A/G	Providencia
TL 4	+	+	-	+	+	+	-	+	+	-	-	A/G	A/G	A/G	Providencia
TH 1A	+	+	-	+	+	+	-	+	-	-	-	A/G	A/G	A/G	Providencia
TH 1B	+	+	-	+	+	+	-	+	+	-	-	A/G	A/G	A/G	Providencia
TH 2A	+	+	-	+	+	+	-	-	+	-	-	A/G	A/G	A/G	Providencia
TH 2B	+	+	-	+	+	+	-	+	+	-	-	A/G	A/G	A/G	Providencia
TH 3	+	+	-	+	+	+	-	+	-	-	-	A/G	A/G	A/G	Providencia
TH 4A	+	+	-	+	+	+	-	+	+	-	-	A/G	A/G	A/G	Providencia
TH 4B	+	+	-	+	+	+	-	+	-	-	-	A/G	A/G	A/G	Providencia
Control group (positive control)															
TC 1	+	+	-	+	+	+	-	-	-	-	-	A/G	A/G	A/G	Providencia

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TC 2	+	+	-	+	+	+	-	+	-	-	-	A/G	A/G	A/G	Providencia
TC 3	+	+	-	+	+	+	-	+	+	-	-	A/G	A/G	A/G	Providencia

Table 5: Biochemical Test Result for Microorganisms isolated from the Gastrointestinal Tract of Wistar rats after Administration of *Eleusinecoracana* Plant Extract

TL: Tamber low dose, TH: Tamber high dose, TC: Tamber control, (+) stands for positive result, (-) stands for negative result, A/G; acid and gas

Groups	**Organisms**	**No of organisms**	**% incidence**
+ve control	*Providencia*	3	100
-ve control	*Aeromonas*	8	25
	Proteus	7	21.9
	Citrobacter	1	3.1
	Pseudomonas	9	28.1
	Staphylococcus aureus	4	12.5
	S. spp	4	12.5
Group 1	*Providencia*	13	100

Table 6: Percentage of Incidence of Identified Bacteria

Group 1: Administered with *Eleusinecoracana* extract and tramadol

IV. DISCUSSION

Utilization of wholegrain cereals in food formulations is increasing worldwide, since they are rich sources of phytochemicals and dietary fiber which offer several health benefits (Jones and Engleson 2010). Millets are important crops in semiarid and tropical regions of the world due to their resistance to pests and diseases, short growing season, and productivity under hardy and drought conditions when major cereals cannot be relied upon to provide sustainable yields. Finger millets are underutilized in many developed countries. There is an immense potential to process millet grains into value-added foods and beverages in developing countries. Furthermore, *Eleusinecoracana*, as they do not contain gluten and hence are advisable for celiac patients (Chandrasekara and Shahidi 2010).

This present study assessed the effect of ethanol extract of *E. coracana* on the gastrointestinal tract (GIT) microbiome of Wistar rats. Table 1 shows the weight of the Wistar rats before and after administration of *E. coracana* plant extracts. The result revealed a significant increase in the weight of the Wistar rats after administration of *E. coracana* plant extract when compared to that of the control group. The result also shows an increase in the weight of Wistar rat administered with high dosage of the plant extract when compared to those administered with low dosage of the extract. The finding is in line with the findings of Eji*et al*. (2020) who reported a significant increase in the body weight of Wistar rats administered with fermented *E. coracana* supplemented with ginger powder. Thus the plant extract of finger millet can serve as treatment of underweight babies and malnourished children following reported that foods for infants should be energy dense because of the limited gastric capacity in young children coupled with the need for increased nutrient intake (Enwa *et al* 2011,Barugahara*et al*., 2015).

The human body harbors trillions of microbial cells whose coordinated actions are believed to be important for human life. Such microbial cell populations reach their highest density in the intestinal compartment, where they collectively form a complex microbial community known as the gut microbiota (Lozupone *et al*., 2012, Enwa *et al* 2016)) which develops over the course of host infancy to eventually reach its adult form (Yatsunenko *et al*., 2012; Yassour *et al*., 2016). Gut microbiota members may belong to any of the three domains of life, i.e., Archaea, Bacteria, and Eukarya, and also include viruses, and they are known to establish complex trophic relationships with each other and their human host, ranging from symbiosis to parasitism (Ventura *et al*., 2009a). The human gut microbiota is composed of autochthonous, also known as indigenous, microorganisms and allochthonous or transient microorganisms (Ventura *et al*., 2009b)

The result as shown in Table 2 and 3 shows the number of colonies counts before and after administration of *E. coracana* plant extract. The results shows a significant decrease in the number of colonies after administration of the high and low dose of *E. coracana* extract. This can be ascribed to the antimicrobial potency of the plant extract. The result also shows a high number of bacterial in the fecal of the Wistar rat than in the GIT, although this was not as high as those found in the control group. The antimicrobial activity of the crude extract of *E. coracana* using different solvents have earlier been reported by a number of researchers showing high antimicrobial activity against microbial strains (Mathanghi and Sudha, 2012; Shukla *et al*., 2015; Singh *et al*., 2015).

Also result presented in Table 4a, 4b and 5 shows different microbial isolates, isolated from the fecal and GIT of Wistar rats and they include; *Aeromonashydrophyla*, *Proteus* spp., *Pseudomonasaeruginosa*, *Citrobacterfreundii*, *S.* spp., *Staphylococcusaureus,* and *Providencia* spp. Before administration of finger millet plant extract, *Aeromonashydrophyla*, *Proteus* spp., *Pseudomonasaeruginosa*, *Citrobacterfreundii*, *S.* spp., *Staphylococcusaureus, C. freundii*,*S.* spp., *S. aureus* and *Providencia* spp. were found in the GIT of the Wistar rats, while on administration of high and low dose of finger

millet plant extract and in combination with tramadol only *Providencia* spp.was found to be present in the GIT of the Wistar rats.

The study revealed that the negative control group contains *Pseudomonas aeruginosa* with percentage incidence of 28.1% (Table 6). This was followed by *A. hydrophyla* and *Proteus* spp., having percentage incidence of 25 and 21.9% respectively. While the least percentage incidence was recorded for *Citrobacterfreundii* (3.1%). The high percentage incidence of *A. hydrophyla* possess serious health challenge to the GIT of the specimen as*P. aeruginosa* infections appear secondary to a breach in host defenses. The translocation of endogenous intestinal *P. aeruginosa* extraluminally is an important pathogenic phenomenon and a cause of systemic infections, especially in neutropenic patients with hematological malignancies (Okuda *et al.*, 2010). During the translocation process, bacteria and their products cross the intestinal barrier by traveling between or through the cells of the intestinal epithelium, causing infection and massive inflammation (Papoff*et al.*, 2012).

More so, *A. hydrophyla* possess serious health challenge to the GIT of the specimen as *A. hydrophyla* has been reported to be an important disease causing pathogen responsible for a number of infectious complications in both immunocompetent and immunocompromised persons (Janda and Abbott, 2010). The occurrence of *C. freundii* found in negative control group may be due to the presence water which encourages microbial growth and the resultant effect causes diarrhea in human **(**Bossi-Küpfere*et al.*, 2007; Janda and Abbott, 2010). The presence of *S. aureus* is can be predicted as *Aeronomas* infection has been reported to be found in association with a number of bacteria including *S. aureus, E. coli* and *K. pneumonia* (Tsai *et al.*, 2006). Although the presence of *C. freundii* in the gut microbiome is associated in healthy species as it acts as an anti-obesity (Schlossing*et al.*, 2013). The effect of this organism can be countered as a result of high percentage incidence of Proteus spp. in the GIT compared to that of the *C. freundii* (Lecomte*et al.*, 2015).

The result also revealed that positive control group had the presence of *Providencia.* spp., with percentage incidence of 100%. The intestinal carriage of *Providencia.* spp. is likely a consequence of the opportunistic nature of this species. Group administered with high and low dose of plant extract in combination with tramadol showed the presence of *Providencia* spp. with a percentage incidence of 100%. The pathology of *Providencia* spp. and strains was defined by Galac and Lazzaro (2011) as the proportion of host mortality caused by the bacteria. The organisms have been described as a possible diarrhea-causing pathogen in travelers and children in developing countries (Yoh*et al.*, 2005).

The study revealed that microbiota influences eating habit on human, this is as a result of the preference of the microbiota which can lead to the host consuming more food which may eventually result into obesity (Schneiderhan*et al.*, 2016). The study revealed that tramadol have an impact on the population of bacteria colonies, this is as a result of the antibacterial property of the opioid, this have been reported in literature showing a decrease in the population of *S.aureus* at a dose of 25mg/mL (Farzam*et al.*, 2018).

V. CONCLUSION

This study assess the effect of ethanol extract of *Eleusinecoracana* on the microbiome gastrointestinal tract of Wistar rats. From the study, it was revealed that the extract of finger millet have effect on the microbiome of the GIT with a reduction in the population of bacteria colonies. The population of the bacterial colonies were reduced drastically on administration of the plant extract and tramadol. The administration of the plant extract also cause an increase in the weight of the Wistar rats, which is as a result of the enhancement of digestion possessed by *E. coracana* plant extract. Owing to this findings, the methanolic extract of *E. coracana* can be administered to malnourished or underweight infants as a food supplement. More so, the plant extract in combination with tramadol can be used as a probiotic and prebiotic, since it alters the microbiome GIT of the Wistar rats, thus serving as an antibacterial agent.

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