THE RISK OF ANTIMICROBIAL RESISTANCE FROM LOW-LEVEL ANTIBIOTIC EXPOSURE IN DIET

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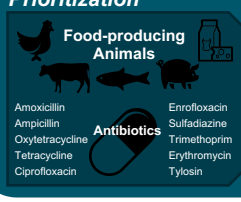
INTRODUCTION

- A wide range of ***antibiotics*** have been widely used in the rearing of ***agricultural animals.***
- ***Extremely limited information is available*** on the antibiotic residues in animal products and the ***adverse impact that consistent low levels of antibiotics*** might have on human body as well is its microbiome.
- The study aim was to ***estimate the possible antibiotic concentration on humans are exposed to thought their diets*** using the concentration of antibiotics in animal products and water, and online survey data of dietary habits.

METHODOLOGY

Prioritization



Online Survey

48-hour recall + Food Frequency questionnaire

Chemical Analysis

LTPE* + LC-MS/MS + Validations

*Low-Temperature Partitioning Extraction

Analysis

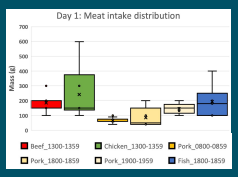
- Dietary habits
- Antibiotic concentration in foods and drinks
- AMR Risk Model

RESULTS & DISCUSSION

Diet Survey

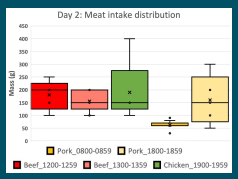
- Different meat consumption trends were observed from the survey (n= 51).

- Most consumed meat types are:



Day1

Breakfast= Pork
Lunch= Chicken
Dinner= Fish



Day2

Breakfast= Pork
Lunch= Beef
Dinner= Chicken

Antibiotic Profiles

- Target antibiotics were detected from the triplicates of 34 food and drink samples.

Antibiotics	TMDI* (ug/person/day; JECFA)	ADI** (ug/kg; JECFA)	LOD (ug/L)	LOQ (ug/L)	R2
Amoxicillin	31.0	2.0	10.3	31.3	0.9995
Ampicillin	31.0	2.0	11.0	33.4	0.9995
Oxytetracycline	370.0	30.0	8.50	25.8	0.9997
Tetracycline	370.0	30.0	10.9	33.2	0.9995
Ciprofloxacin		2.0	8.93	27.1	0.9996
Enrofloxacin		2.0	11.7	35.5	0.9994
Sulfodiazine	87.5	50.0	8.32	25.2	0.9997
Trimethoprim		4.2	12.5	38.0	0.9993
Erythromycin	27500.0	700.0	5.75	17.4	0.9999
Tylosin	230.0	30.0	10.0	30.4	0.9996

*Theoretical Maximum Daily Intake
**Acceptable Daily Intake

- 12 out of 34 products had **exceeded ADI*** antibiotic concentration.

Product Type	Product Name	Average Weight (g)	Penicillin (µg) Amoxicillin	Penicillin (µg) Ampicillin	Fluoroquinolone (µg) Enrofloxacin
Beef	Minced	200	322.3	126.6	
	Rump	150	155.1	197.8	
	Sirloin	200	129.2	131.9	135.0
	Ribeye	150	134.9	237.3	123.4
	Burger Patty	200		141.7	289.3
Chicken	Thigh	200	307.0		
	Breast	250	355.3		
	Drumstick	150	210.5		
Pork	Ham	90	214.9		
	Sausage	80			439.8
	Salami	70	480.7		295.4
Dairy	Semi-skimmed milk	180	136.8		

*ADI= Acceptable Daily Intake

Antibiotic Intake Estimation

- Estimated Daily Intake (EDI; FDA, 2021) formula was modified to our study **to calculate antibiotic intake from each meal (Estimated Meal Intake; EMI).**

$$\sum_{f=1}^{F}\left\{\frac{\text{Portion}f \times \text{Concentration } x \, f \times \text{Frequency } f}{N} \times \frac{\text{portion } f}{V \text{ total}}\right\}$$

Where,
F = Total number of foods in which antibiotic "*x*" can be found
Portion f = Average portion size for food "*f*"
Concentration x f = Concentration of the substance "*x*" in food "*f*"
Frequency f = Number of eating occasions of food "*f*" over "*N*" meals in during the survey
N = Number of meals
V total = Average volume of drinks + Average volume of meal + Average gut juice (60ml)

Day1

Breakfast (Pork)
- AMOX* (141.3 µg/ml)
- ENR* (64.2 µg/ml)

Lunch (Chicken)
- AMOX (399.4 µg/ml)

Dinner (Fish)
- <ADI

Day2

Breakfast (Pork)
- AMOX (132.5 µg/ml)
- ENR (80.3 µg/ml)

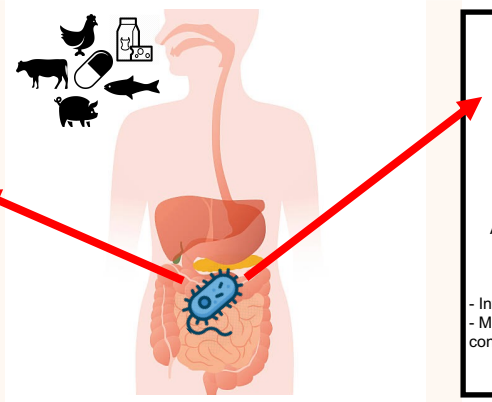
Lunch (Beef)
- AMOX (170.7 µg/ml)
- AMP* (193.5 µg/ml)
- ENR (194.4 µg/ml)

Dinner (Chicken)
- AMOX (408.1 µg/ml)

*AMOX= Amoxicillin; AMP= Ampicillin; ENR= Enrofloxacin

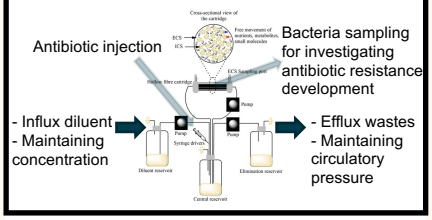
CONCLUSION

1. **Amoxicillin, Ampicillin and Enrofloxacin** were calculated as residues which could impact the gut microbiome via diet.
2. **High potential of developing antimicrobial resistance** because the calculated antibiotic concentration outcomes are **found within the range of MICs of *E. coli*** reported on the EUCAST (2022) MIC database.



FUTURE WORK

Simulating the diet habit results by exposing human gut bacteria to the calculated antibiotic concentrations at each meal using Hollow Fibre Infection Model (Maitra et al., 2021)



REFERENCES

EUCAST (2022). *MIC EUCAST*. [online] mic.eucast.org. Available at: https://mic.eucast.org/search/?search%5Bmethod%5D=mic&search%5Bantibiotic%5D=-1&search%5Bspecies%5D=261&search%5Bdisk_content%5D=-1&search%5Blimit%5D=50 [Accessed 26 Apr. 2022].

FDA (2021). *Guidance for Industry: Estimating Dietary Intake of Substances in Food*. [online] U.S. Food and Drug Administration. Available at: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/guidance-industry-estimating-dietary-intake-substances-food [Accessed 26 Apr. 2022].

Maitra, A., Solanki, P., Sadouki, Z., McHugh, T.D. and Kloprogge, F. (2021). Improving the Drug Development Pipeline for Mycobacteria: Modelling Antibiotic Exposure in the Hollow Fibre Infection Model. *Antibiotics*, 10(12), p.1515.

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