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Evaluation of antibiotic potential of metabolic peptides derived from gut microbial samples using in Silico Approach

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ABSTRACT

The antibiotic potential of metabolic peptides derived from Camel gut microbial sample is evaluated in this study using computational methods. Data on sequence of microbes isolated from the digestive system of Camel was retrieved from the sequence raw archive (Accession number SRR 13205865) of National Centre for Biotechnology Information. The retrieved sequence was subjected to genome assembly using the database of Bacterial Viral Bioinformatics Resource Centre. Identification of secondary metabolites was done using Anti SMASH server. The identified metabolic peptides include arylpolyene, phosphonate and NRPS. The antibiotic potential of the secondary metabolites was predicted using CAMPR3 server. The antibiotic potential of different regions of the metabolic peptides was predicted the antibacterial peptide prediction server. The result indicated positive antimicrobial potential of the secondary metabolites derived from microbes isolated from camel digestive system. Further research on the therapeutic potential of the identified metabolic peptides for the treatment of bacterial infections is recommended.

***Keywords: antibiotic potential, camel gut microbial, biotechnology information, metabolic peptides*.**

INTRODUCTION

Spread of antibiotic resistant bacteria has been identified as a global public health threat (**Evelina *et al.*, 2018**). There is significant increase in antimicrobial resistance as a result of misuse of antibiotics in health care and agriculture, this major public health concern result in high mortality worldwide due to drug resistant infections (**Marcus *et al.*, 2021**). Development of new antimicrobial agents is required to improve the treatment outcome of infectious diseases and save lives (**Danquah *et al.*, 2022**).

Microorganisms are potential reservoirs for biomolecules with structural and functional antimicrobial activity; they are important sources of bioactive compounds with antimicrobial, anti-fungal and cytotoxic bioactivity. Their therapeutic potential is due to the production of rich secondary metabolites (**Elissawy *et al.*, 2021**). Researchers have recently given attention to microbes as potential source of novel antimicrobial agents due to the biological properties secondary metabolites produced by microbes. Antimicrobial peptides are produced naturally by microorganisms as part of their innate immune system against pathogens, they have the potential to inhibit protein and nucleic acid synthesis leading to necrosis and apoptosis (**Pfalzgraff *et al.*, 2018**). Development of antimicrobial agents from microbial sources is facilitated by advances in molecular biology and computational technologies (**Maghembe *et al.*, 2020**). The World Health Organization (WHO) reported that antibiotic pipelines are not sufficient to meet the growing antimicrobial resistance; there is a need to for improved investment in the discovery and development of novel antibiotics (**Anderson *et al.*, 2023**). The main objective of this study was to computationally evaluate the antibiotic potential of secondary metabolites derived from microorganisms isolated from the digestive tract of camel.

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MATERIALS AND METHODS

Data retrieval and genome assembly

Data on sequence of microorganism derived from camel gastrointestinal tract was retrieved from Sequence Raw Archive of National Centre for Biotechnology Information (NCBI). The sequence was subjected to genome assembly using the database of Bacterial Viral Bioinformatic Resource Centre. BV-BRC is an information system design to support research in bacterial and viral infection diseases (**Olson *et al.*, 2023**). It is a merger of path systems research integration center (PATRIC), the influenza research database (IRD) and the virus pathogen database and analysis resources.

Identification of secondary metabolites

The secondary metabolites produced by the microorganisms were identified using the antiSMASH database as described by **Blin *et al.*, 2023**. It is a comprehensive database of microbial secondary metabolite biosynthetic gene clusters (**Blin *et al.*, 2017**). It is a multilayer web server implanted in Python using the flask framework.

Prediction of antimicrobial probability of metabolic peptides

The antimicrobial activity of the metabolic peptides was predicted using CAMPR3 (collection of antimicrobial peptide) database as described by (**Waghu *et al.*, 2016**). It is a database of specific signatures of antimicrobial peptides integrated with tools for AMP sequence and structure analysis. The database provide comprehensive information on AMPS and machine learning based predictive models.

Prediction of antibiotic activity

Antibacterial activity of the peptide sequences was predicted using antibacterial peptide server. The server predicts antibacterial peptide in a sequence with an overall accuracy of 92.11 % (**Lata *et al.*, 2007**). Prediction can be done using artificial neural network (ANN), quantitative matrix (QM) and support vector machine (SVM).

RESULTS AND DISCUSSION

The antimicrobial peptide probability of the metabolic peptides was predicted using CAMPR3 as shown in Table 1.

Table 1: Prediction of Antimicrobial potential of Secondary metabolites derived from Camel gut microbes using CAMPR3.

Secondary metabolites	Amino acid sequences	Antimicrobial peptide probability			
		SVM	RF	ANN	DF
Arylpolyene	LTLSSIFGIGGLSVTVSAAC	0.83	0.88	AMP	0.87
Phosphonate	IIAANEGGAMGIAAGHYLAT	0.54	0.68	AMP	0.68
NRPS	GLDVKTSEILRKPAIRAWIN	0.73	0.85	AMP	0.87

SVM- Support Vector Machine, RF - Random Forest, ANN - Artificial Neural Network, DF - Discriminant Analysis, NAMP- Non antimicrobial peptide, AMP - Antimicrobial peptide.

All peptide sequences evaluated indicated significant antimicrobial probability with arylpolyene demonstrating the highest antimicrobial peptide probability.

The antibacterial activity of the metabolic peptides was predicted using the anti-Bacterial Peptide server.

The highest recorded antibiotic activity of the secondary metabolite peptide was 0.579.

Table 2: Prediction of antibiotic activity of peptides derived from Camel gut metagenomic samples using Anti BP Server.

PEPTIDE	Start position	Score	Antimicrobial activity
LTLSSIFGIGGLSVTVSAAC	1	- 0.801	NO
SIFGIGGLSVTVSAA	5	0.579	YES
IIAANEGGAMGIAAG	1	0.124	YES
NEGGAMGIAAGHYLA	5	0.222	YES
GLDVKTSEILRKPAIRAWIN	1	0.539	YES
DVKTSEILRKPAIRA	3	0.333	YES
KTSEILRKPAIRAWI	5	0.330	YES

Antibiotic resistant bacteria posed a significant threat to global health necessitating the development of new effective therapeutics. These molecules exhibit broad spectrum antimicrobial activity, low toxicity and reduced microbial resistance (**Waghu and Thomas, 2019**). Antimicrobial peptides (AMPS) are host defense molecules produced by a wide range of microorganisms. AMPs act through various mechanisms such as destruction of microbial membranes and inhibition of macromolecule synthesis. This multiple mechanism of action makes it difficult for microbes to develop resistance against amps as compared to conventional antibiotics (**Roy *et al.*, 20**15). Metabolic products of microorganism are commonly used in the development of drugs and crop protection products. Genome mining has provided a great opportunity to assess the potential of secondary metabolites produced by microbes (**Blin *et al.*, 2023**). Microbial secondary metabolites are main source of bioactive compounds used as antimicrobial and anticancer drugs. Significant number of antibiotics in clinical use is derived from products of microorganisms and plants (**Blin *et al.*, 2017**). The discovery and design of antimicrobial peptides is aided by the family specific sequence composition of antimicrobial peptides. The family signatures are used to accelerate the discovery of AMPs (**Waghu *et al.*, 2016**).

Findings of this study indicated insilico evaluation of the secondary metabolites derived from microorganisms isolated from gastrointestinal tract of camel demonstrated antibiotic activity. Further research on design of antibiotics using metabolic peptides derived from camel gut microorganisms is recommended.

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