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An Insight into the Structure-Activity Relationship of Antimicrobial Peptide Brevinin

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ABSTRACT

Numerous amphibian species, particularly those of the genus Rana, have been found to produce linear, amphiphilic, and cationic antimicrobial peptides (AMPs). Such AMPs are gaining more attention in pharmaceutical applications due to their principal method of action, which involves penetrating and rupturing the intended cell membranes with relatively low resistance. Brevinin is a large family of AMPs extensively studied during the last few decades, primarily consisting of two groups of peptides: Brevinin-1 and Brevinin-2. These peptides are cationic and establish secondary structures in the biological membrane environment. In this discussion, we explore the effects of structural parameters (net charge, hydrophobicity, amphiphilicity, helicity, peptide length, etc.) of Brevinin on their antimicrobial activity. As a general rule, an increased net charge tends to enhance antimicrobial activity. However, it is important to note that excessive net charges can also elevate hemolytic activity. The amino acid composition significantly influences hydrophobicity and helicity, which, in turn, impact the activity of the peptides. Moreover, these structural parameters are interconnected; modifying one parameter will affect others. Striking an optimal balance in these factors will provide a Brevinin analog with the highest antimicrobial activity and the lowest hemolytic activity.

Keywords: Antimicrobial peptides; Brevinin; Helicity; Hydrophobicity; Net charge; Hemolytic activity.

1. INTRODUCTION

The irrational use of antibiotics contributes to antimicrobial resistance in infectious pathogens, posing a severe global public health concern [1]. Increased antimicrobial resistance has resulted in the failure of traditional medicine to treat conditions effectively, heightened infection risks, prolonged hospital admissions, and, ultimately, an economic burden on nations [2, 3]. Therefore, it is vitally necessary to develop active antimicrobial compounds with lower resistance levels.

Antimicrobial peptides (AMPs) play a significant role in combating resistant microbes due to their rapid and broad-spectrum effectiveness against fungi, viruses, and both Gram-positive and Gram-negative bacteria [4, 5]. In contrast to conventional antibiotics, AMPs bind to the bacterial membrane, causing disruption rather than targeting a specific site. The barrel-stave, carpet, or toroidal models are employed to describe the membrane disruption caused by AMPs [6-8], making it challenging for microorganisms to develop resistance against them [9].

AMPs are typically small, naturally occurring peptide molecules consisting of 10 to 50 amino acids. Most AMPs carry a net positive charge at physiological pH due to the presence of basic amino acids, facilitating electrostatic interactions with the membranes of negatively charged microorganisms [10]. An important structural feature of these peptides is amphiphilicity, characterized by the presence of hydrophobic residues on one side and hydrophilic residues on the other side of the molecule [11]. Amphiphilicity also aids in binding to the hydrophobic and hydrophilic regions of the target pathogen. In the presence

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of lipid membranes, many AMPs adopt a distinct secondary structure, such as α-helix or β-sheet, essential for antibacterial activity [12, 13].

AMPs are ubiquitous in almost every living organism, serving as a component of their innate immune system. Extracted from the skin of amphibians, these AMPs have demonstrated superior efficacy against microorganisms, offering a potential solution to current antimicrobial resistance problems [14].

Amphibian AMPs are categorized into peptide families, including brevinins, cathelicidin, temporins, esculentin, ranatuerin, etc., based on shared structural properties and their ability to combat pathogens [15]. Brevinin (Figure 1) is a crucial amphibian AMP family isolated from the Ranidae, exhibiting high biological activities and distinctive structural properties [16]. Originally identified in Rana brevipoda porsa [17], hundreds of Brevinin peptides have been discovered and their data deposited in the database [18]. These peptides exhibit various bioactivities, encompassing antimicrobial, anticancer, hypoglycemic, anti-inflammatory, and more [19].

Researchers have designed numerous Brevinin analogs, aligning with common AMP features and the predicted secondary structure of peptides, to explore the structure-activity relationship and enhance their antimicrobial activity. For instance, Lin et al. extracted Brevinin-2GUb from the skin secretion of Hylarana guentheri, producing analogs to investigate its cationic activity [20]. The augmentation of cationic charges significantly enhances the compound's bioactivity while mitigating its toxicity effects. AMPs exhibit various structural parameters (amphiphilicity, net charge, charge density, length, hydrophobicity, hydrophobic moment, and helicity) influencing antimicrobial activity. Hence, this study delves into the structural features of Brevinin analogs and the impact of structural changes on their antimicrobial activity. Understanding the structural activity relationship of Brevinins is crucial for identifying the most effective peptide to serve as a template for developing new antimicrobial agents with medicinal properties.

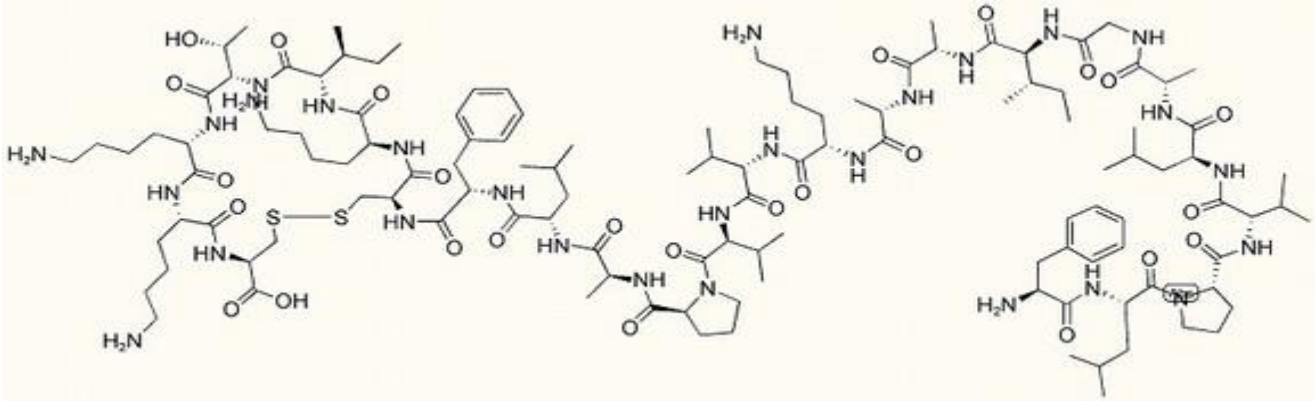


Figure 1. Chemical structure of Brevinin-1

2. Importance of SAR study of Brevinin

A structure-activity relationship (SAR) study is crucial for understanding the correlation between structural parameters and the antimicrobial activity of peptides. Researchers can create synthetic analogs of parent peptides to enhance antimicrobial efficacy. For example, synthetic hybrid peptides derived from natural indolicidin and ranalexin exhibit greater antibacterial activity compared to their parent analogs against Streptococcus pneumoniae [21]. Larger antimicrobial peptides may demonstrate increased hemolytic tendencies, whereas shorter peptides with higher cationic content tend to reduce hemolytic activity [22].

An in-depth exploration of peptide structure is essential

for the rational design of α-helical AMPs with heightened antimicrobial activity and specificity [23]. Examining the SAR of AMPs is also vital for comprehending the diverse mechanisms responsible for the antimicrobial activities of peptides [24]. It is imperative for researchers to expand SAR studies to unearth novel peptide analogs with enhanced antimicrobial activity. Brevinin, a substantial group of AMPs, exhibits a broad-spectrum activity against bacteria, viruses, fungi, and other parasites (Table 1). Understanding the structure-activity relationship of Brevinin is pivotal for discovering more bioactive analogs, contributing to advancements in medical science.

Table 1. Some notable Brevinin family AMPs with their sequences, sources, and major bioactivities

Name	Length	Amino Acid Sequence*	Bioactivities	Source	References
Brevinin-1	24	FLPVLAGIAAKVVPALFCKITKKC	Antibacterial, high hemolytic activity	*Rana brevipoda porsa*	[17]
Brevinin-1AVa	17	FLPLLAASFACTVTKKC	Antibacterial	*Rana arvalis*	[25]
Brevinin-1Ba	24	FLPFIAGMAAKFLPKIFCAISKKC	Antibacterial	*Lithobates berlandieri*	[26]
Brevinin-1BYa	24	FLPILASLAAKFGPKLFCLVTKKC	Antibacterial, antifungal and hemolytic activity	*Rana boylii*	[27]
Brevinin-1CDYa	20	LLSLALAALPKLFCLIFKKC	Antibacterial and weak hemolytic activity	*Rana chensinensis*	[28]
Brevinin-1CG1	24	FLSTALKVAANVVPTLFCKITKKC	Antibacterial, antifungal and low hemolytic activity	*Amolops chunganensis*	[29]
Brevinin-1CSa	24	FLPILAGLAAKIVPKLFCLATKKC	Antibacterial and strong hemolytic activity	*Rana cascadae*	[30]
Brevinin-1DYb	20	FLSLALAALPKLFCLIFKKC	Antibacterial, antifungal, anticancer, candidacidal and strong hemolytic activity	*Rana dybowskii*	[31]
Brevinin-1E	24	FLPLLAGLAANFLPKIFCKITRKC	Antibacterial	*Pelophylax saharicus*	[32]
Brevinin-1HN1	24	FLPLIASLAANFVPKIFCKITKKC	Antibacterial, antifungal, candidacidal and low hemolytic activity	*Odorrana hainanensis*	[33]
Brevinin-1HSa	24	FLPAVLRVAAKIVPTVFCAISKKC	Antibacterial activity	*Odorrana hosii*	[34]
Brevinin-1ITa	20	IVPFLLGMVPKLVCLITKKC	Antibacterial, cytotoxic and hemolytic activity	*Rana italica*	[35]
Brevinin-1OKa	22	FFGSMIGALAKGLPSLISLIKK	Antibacterial	*Rana okinavana*	[36]
Brevinin-1OKc	22	FFGSIIGALAKGLPSLISLIKK	Antibacterial	*Rana okinavana*	[36]
Brevinin-1Pa	24	FLPIIAGVAAKVFPKIFCAISKKC	Antibacterial, antifungal and candidacidal activity	*Rana pipiens*	[26]
Brevinin-1PLb	24	FLPLIAGLAANFLPKIFCAITKKC	Antibacterial, antifungal and candidacidal activity	*Lithobates palustris*	[37]
Brevinin-1Ra	24	VIPFVASVAAEMMQHVYCAASRRC	Antibacterial	*Pelophylax ridibundus*	[38]

Name	Length	Amino Acid Sequence*	Bioactivities	Source	References
Brevinin-1Sa	24	FLPAIVGAAGQFLPKIFCAISKKC	Antibacterial and antifungal activity	*Rana sphenocephala*	[39]
Brevinin-1SE	23	FLPLVRGAAKLIPSVVCAISKRC	Antibacterial activity	*Rana sevosa*	[40]
Brevinin-1SN1	24	FLPAVLKVAAHILPTAICAISRRC	Antibacterial and hemolytic activity	*Hylarana spinulosa*	[41]
Brevinin-1SPa	24	FFPIIAGMAAKLIPSLFCKITKKC	Antibacterial, antifungal, candidacidal and hemolytic activity	*Lithobates septentrionalis*	[42]
Brevinin-1T	20	VNPIILGVLPKFVCLITKKC	Antibacterial, high hemolytic activity	*Rana temporaria*	[43]
Brevinin-2	33	GLLDSLKGFAATAGKGVLQSLLSTASCKLA KTC	Antibacterial, high hemolytic activity	*Rana brevipoda porsa*	[17]
Brevinin-2DYe	37	GLFSVVTGVLKAVGKNVAKNVGGSLLEQL KCKISGGC	Antibacterial	*Rana dybowskii*	[31]
Brevinin-2GHb	30	GVITDALKGAAKTVAAELLRKAHCKLTNSC	Antibacterial	*Rana guentheri*	[44]
Brevinin-2GHc	31	SIWEGIKNAGKGFLVSILDKVRCKVAGGCN P	Antibacterial	*Hylarana guentheri*	[44]
Brevinin-2GRa	33	GLLDTFKNLALNAAKSAGVSVLNSLSCKLS KTC	Antibacterial, antifungal, candidacidal and hemolytic activity	*Odorrana grahami*	[45]
Brevinin-2ISa	33	SLLDTFKNLAVNAAKSAGVSVLNALSCKISR TC	Antibacterial, Antifungal and candidacidal activity	*Odorrana ishikawae*	[46]
Brevinin-2JD	33	GLLDTFKNLALNAAKSAGVSVLNSLSCKLS KTC	Antibacterial, antifungal, candidacidal and weak hemolytic activity	*Odorrana jingdongensis*	[47]
Brevinin-2LT	33	GLMSVLKKAGKHVAKNVAASLMDSLKCKI TGGC	Antibacterial	*Rana latastei*	[48]
Brevinin-2R	25	KLKNFAKGVAQSLLNKASCKLSGQC	Antibacterial, antifungal, anticancer, candidacidal activity	*Pelophylax ridibundus*	[49]
Brevinin-2Ra	29	GILDSLKNFAKDAAGILLKKASCKLSGQC	Antibacterial	*Pelophylax ridibundus*	[50]
Brevinin-2Ta	33	GILDTLKNLAKTAGKGILKSLVNTASCKLSG QC	Antibacterial, antifungal, candidacidal, anti-inflammatory and wound-healing activity	*Pelophylax kl. esculentus*	[51]
Brevinin-Eu	24	VIPFVASVAAEMMQHIFCAASRKC	Antibacterial, very low hemolytic activity	*Euphlyctis cyanophlyctis*	[52]
Brevinins-ALa	24	FLPMLAGLAANFLPKLFCKITKKC	Antibacterial, antifungal, and strong hemolytic activity	*Amolops loloensis*	[53]

*Refer to **table S1** in the appendix

3. Structural features of Brevinin

The Brevinin family is divided into two subfamilies: Brevinin-1 and Brevinin-2. Brevinin-1 (FLPVLAGIAAKVVPALFCKITKKC) comprises approximately 24 residues, while Brevinin-2 (GLLDSLKGFAATAGKGVLQSLLSTASCKLAKTC) has a length of approximately 33 residues. Brevinin-1 exists in two forms: cyclic and acyclic Brevinin-1 [36]. Acyclic

Brevinin-1 lacks Cys residues but has an amidated C-terminus, while cyclic Brevinin-1 features a disulfide bond at its C-terminus. Although the primary structure of Brevinins may vary among species, they typically contain a highly conserved portion in the 'Rana box' sequence. The Rana box is usually situated at the C-terminus, and its structure is [Cys18-(Xaa)4-Lys-Cys24] for Brevinin-1 [54]. While the length and amino acid composition of the peptides may vary, they all carry a net positive charge at neutral pH. Bacterial cell membranes, lacking neutral and zwitterionic lipids compared to mammalian cell membranes, make it easier for Brevinins to selectively attach to the anionic phospholipids of bacterial cell membranes [55].

Brevinins typically exist as randomly arranged coils in an aqueous solution but adopt an amphipathic α-helical shape in environments that mimic hydrophobic membranes, such as 50% trifluoroethanol (TFA) [56]. The peptide structure and the side chains of Brevinin-1 in a 33% trifluoroethanol solution are depicted in Figure 2. The α-helical structure is believed to disturb the phospholipid bilayer of the targeted membranes under such circumstances.

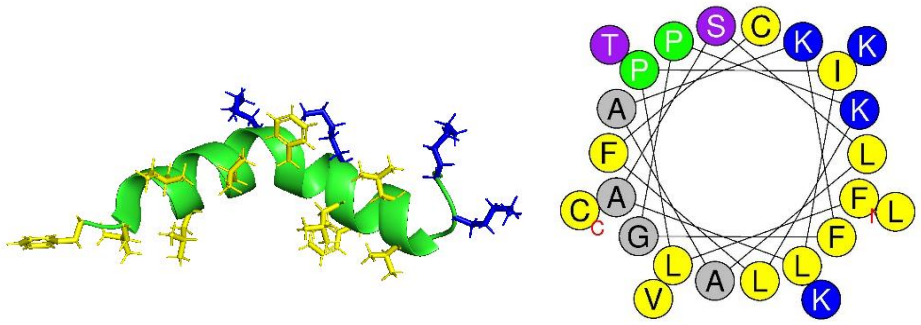


Figure 2. Structure of Brevinin-1BYa. (A) The solution NMR structure of Brevinin-1BYa in 33% trifluoroethanol (PDB ID: 6G4I) visualized in PyMOL (version 2.4.1.), (B) Helical wheel representation of Brevinin-1BYa obtained from HeliQuest server (https://www.heliquest.ipmc.cnrs.fr/). The positively charged, negatively charged, hydrophobic, and hydrophilic amino acids are each represented by a different color: blue, red, yellow, and purple, respectively. The letters 'N' and 'C' stand for the N-terminal and C-terminal, respectively.

3.1. Net charge

The peptides belonging to the Brevinin family are cationic. Typically, the positively charged residues (arginine, lysine), combined with negatively charged residues (aspartate, glutamate) in the peptide sequence, are totaled to determine the net charge of a peptide. The positive charge of the peptide molecule plays a crucial role in binding to the negatively charged surface of microorganisms [57]. Previous studies suggest that cationic peptides need a net charge of at least +2 to exhibit antibacterial effects effectively [58]. In general, higher net charge enhances the antibacterial action of peptides. For instance, Brevinin-2PTb (charge +5) demonstrates greater antimicrobial activity than Brevinin-2PTc (charge +4) and Brevinin-2HSa (charge +3) against E. coli 25726 [36]. However, it's essential to note that the impact of net charge is not always linear with activity. Another critical consideration is that an increased net charge of the peptide

also escalates hemolysis of human red blood corpuscles. Figure 3 illustrates the effects of net charge on the activity of various peptides [59, 60, 41].

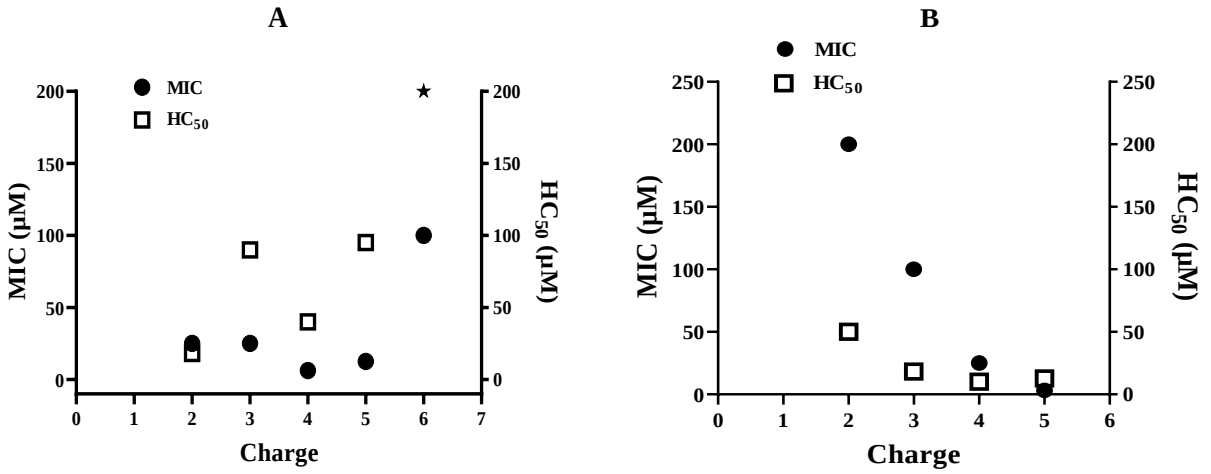


Figure 3. Relationship between charge and antimicrobial & hemolytic activity of Brevinin-2 related peptides (A) and Brevinin-1 peptides (B). The antimicrobial activity was measured in minimal inhibitory concentration (MIC) against *Staphylococcus aureus* 25923. The hemolysis of 50% human red blood cell concentration was considered as HC_{50}. ⋆ A marked point indicates a value greater than that point (>200µM).

Figure 3A illustrates that a peptide with a net charge of +4 exhibits the most potent antimicrobial activity, while one with a net charge of +2 shows hemolytic activity. Additional research by Islam et al. emphasizes that the optimal charge selection is crucial in peptide design to achieve maximum antimicrobial activity with minimal hemolysis [61]. In this context, we also observe that peptides with net charges of +3 and +5 display superior antimicrobial action with considerably low hemolytic activity.

Conversely, Figure 3B demonstrates that a peptide with a net charge of +5 has the best antimicrobial activity with the lowest hemolytic activity.

3.2. Hydrophobicity

The hydrophobicity of a peptide is measured by the solubility of its amino acids in water. The composition of a peptide determines its hydrophobicity, with a higher proportion of hydrophobic residues making the peptide more hydrophobic and vice versa.

The hydrophobicity of an AMP is a critical factor for its insertion into the pathogen's membrane. Trp, a hydrophobic amino acid, enhances its ability to bind to lipids, influencing the interfacial region of lipid bilayers [62]. A hydrophobicity threshold is presumed to play a role in selective bacterial membrane insertion and subsequent cell death. However, increased peptide hydrophobicity is associated with higher hemolytic activity [63]. In a previous investigation, Brevinin-2PRc and Brevinin-2PRd showed lower toxicity against red blood cells because their hydrophobicity decreased when Phe was replaced with Leu [64]. Another study demonstrated a linear relationship between hydrophobicity and hemolytic activity [65]. Thus, scrutinizing peptide hydrophobicity is crucial to avoid hemolysis. In Figure 3, we depict the relationship between the hydrophobicity of several Brevinin peptides and their

antimicrobial and hemolytic activity [66, 29]. The peptides share similar net charges and lengths, and their hydrophobicity values were calculated using HeliQuest.

In Figure 4A, it is shown that peptides with lower hydrophobicity values exhibit lesser antimicrobial activity, with the optimal action observed at 0.75; beyond this point, increasing hydrophobicity leads to a reduction in activity. The diminished activity of highly hydrophobic peptides is attributed to their self-aggregation, preventing them from passing through the microbial cell wall [63].

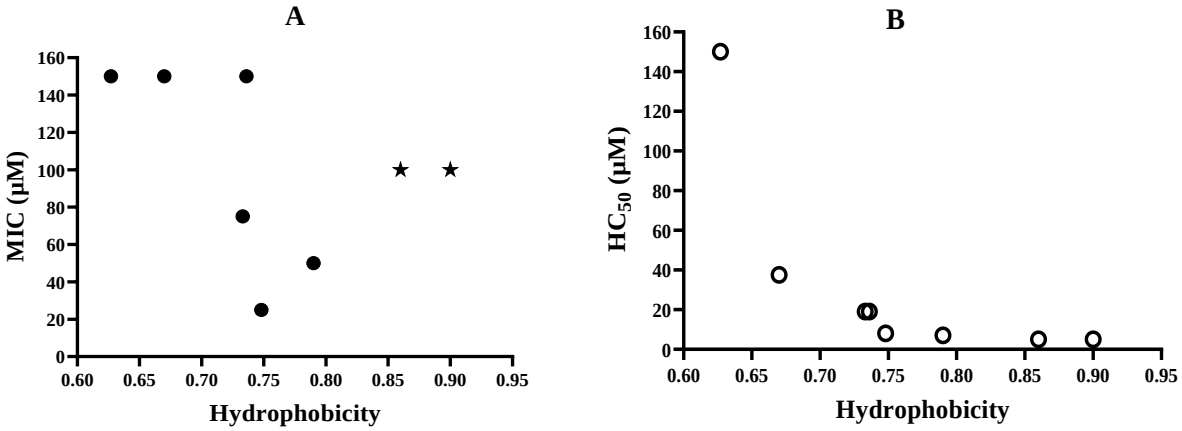


Figure 4. Relationship among hydrophobicity and antimicrobial activity (A) and hemolysis (B) of Brevinin peptides. The antimicrobial activity was measured in minimal inhibitory concentration (MIC) against *Escherichia coli* 25922. The *hemolysis of 50% human red blood cell concentration was considered as HC_{50}. Marked points indicate values greater than that point (>100µM).

Hemolytic activity demonstrates a direct proportionality to the hydrophobicity value of Brevinin peptides (Figure 4B). Given these two phenomena, it is advisable to design peptides with hydrophobicity that promotes antimicrobial activity while concurrently minimizing hemolytic activity.

3.3. Peptide length

The length and amino acid composition of Brevinins vary, but they all feature a distinctive "Rana Box" at the C-terminus, where positively charged residues cluster. Kumari and Nagaraj demonstrated that the disulfide bridge and the cationic cluster at the C-terminus of Brevinin 1E have no impact on antimicrobial activity but do affect hemolytic activity. Peptides lacking a disulfide bridge at the 'Rana Box' exhibit lower hemolytic activity due to a loss of rigidity [67]. Conversely, the activity of Brevinin-1GHa was diminished by removing the Rana Box from the C-terminus [68]. This reduction in activity may be attributed to a decrease in helicity. The N-terminal end of Brevinin-2GUb contains active fragments from the first to the nineteenth amino acids. However, the amino acid composition should offer sufficient hydrophobicity and net charge for interaction with the microbial membrane [20]. Despite being a 12-amino-acid-containing peptide, Brevinin-1OSf exhibits superior antimicrobial and lower hemolytic activity compared to Brevinin-1OS (24 amino acids) [69]. A C-terminus truncated peptide, Brevinin-2GK (1-25), demonstrated higher antibacterial activity than the parent Brevinin-2GK (33 residues), despite having less hemolytic activity. This suggests that the N-terminal helical segment of Brevinin-2GK is the primary cause of membrane rupturing [70].

It is evident that maintaining a balance between α-

helicity, positive charge, and hydrophobicity, rather than peptide length, is crucial for effective antibacterial activity.

3.4. Amphiphilicity

The amphiphilic nature of a peptide is essential for membrane activity [11]. This characteristic enables the interaction with lipid heads on the membrane and deep insertion into the membrane by segregating hydrophobic residues to one side of the helix.

Analog studies of Brevinin-1OS demonstrated a direct proportionality between amphiphilicity and the antimicrobial and hemolytic activity of peptides [69]. Figure 5 illustrates the linear relationship between the amphiphilicity index and the activity of four Brevinin-1 analogs (OSc, OSd, OSe, and OSf).

Among these peptides, the one with the lowest amphiphilicity exhibits the lowest activity (high MIC and HC50 values). Activity against microbes and red blood cells increases with the rise in amphiphilicity. Therefore, selecting a peptide with high antimicrobial activity and considerably low hemolytic activity is of utmost importance.

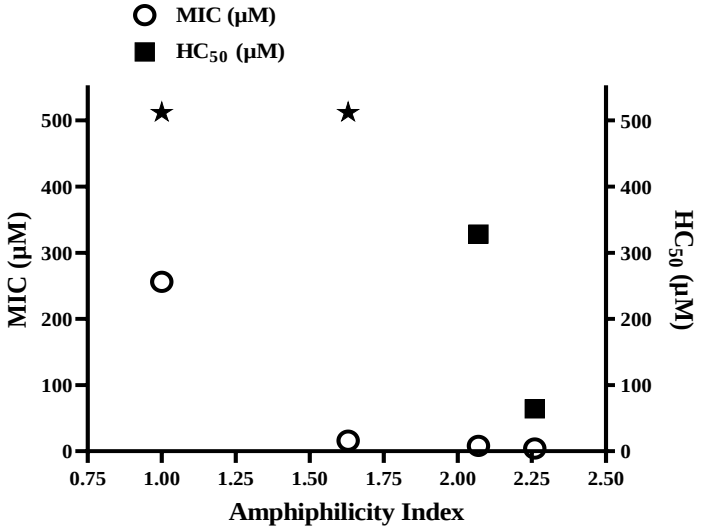


Figure 5. Relationship between amphiphilicity index and activity of four Brevinin-1 analogs. The amphiphilicity index is obtained from the Database of Antimicrobial Activity and Structure of Peptides (https://dbaasp.org/home). The MIC value was measured against *Staphylococcus aureus* (NCTC 10788), and HC_{50} was considered as the concentration required for the hemolysis of 50% of horse red blood cells. Marked points indicate values greater than that point (>512µM for HC_{50}).

3.5. Helicity

Helicity refers to the ability of an antimicrobial peptide to adopt a helical structure in a specific environment, such as negatively charged phospholipids in the bacterial cell membrane. Increased helicity enhances antimicrobial activity, selectivity, and stabilizes the α-helical structure. The combination of α-helicity and hydrophobicity is heightened by a cationic charge, which, in turn, increases hemolytic activity compared to antimicrobial activity [71].

While the structural properties of peptide α-helices may be crucial for bacterial cell death, their content may not directly correlate with antibacterial efficacy [72]. For

instance, OSd, due to the formation of a greater amount of α-helical composition than OSc, exhibits significantly increased antibacterial activity. Despite a more pronounced α-helical structure, OSd is less effective in inhibiting bacterial growth compared to both OSe and OSf, which have lower helicity [69].

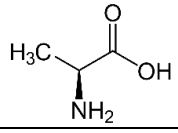
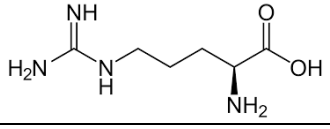
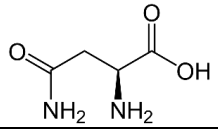
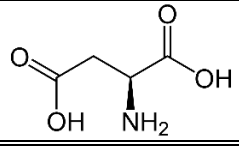
Analog studies of Brevinin-2GUb revealed reduced ability to generate a secondary structure (α-helix) in the analogs, resulting in lower activity on both the microbial surface and red blood cells [68]. A similar outcome was observed for B1CTcu1, where the peptide's binding affinity to the bacterial membrane and hemolytic activity were relatively low due to its diminished capacity to adopt an α-helical structure [73].

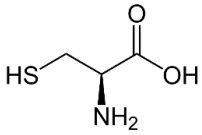
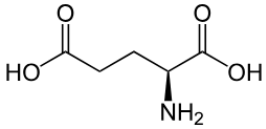
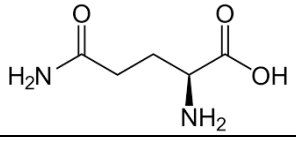
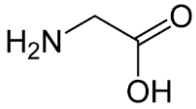
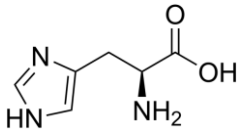
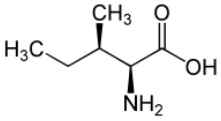
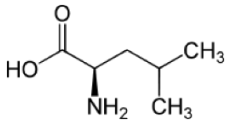
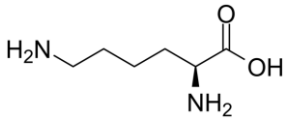
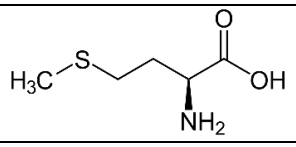
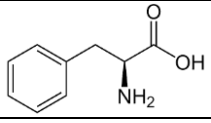
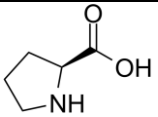
4. CONCLUSION

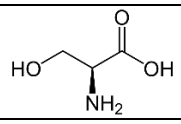
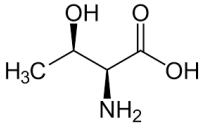
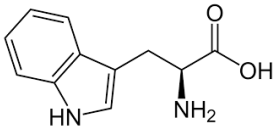
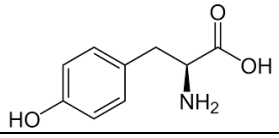
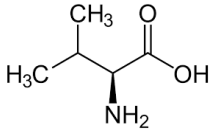
Antimicrobial peptides (AMPs) represent a promising alternative to traditional antibiotic molecules due to their remarkable activity against pathogenic species. Amphibian skin serves as an excellent source of animal AMPs, with Brevinin being a well-studied peptide over the past few decades. The activity of Brevinins can be modulated by manipulating various structural features. The net charge exhibits a direct relationship with activity, while hydrophobicity and α-helicity are predominantly associated with hemolytic activity. However, designing an active peptide requires consideration of multiple parameters. Positive charge, hydrophobicity, α-helicity, and amphipathicity interact intricately to delineate the cytolytic actions of Brevinins against both bacteria and mammalian cells. This study contributes to the design of novel, functional antimicrobial molecules with potential therapeutic applications.

Conflict of interest statement: The authors declared no conflict of interest.

Table S1: Amino acid coding system.

Amino acid name	Abbreviation	Single letter abbreviation	Structure
Alanine	Ala	A	
Arginine	Arg	R	
Asparagine	Asn	N	
Aspartic acid	Asp	D	

Amino acid name	Abbreviation	Single letter abbreviation	Structure
Cysteine	Cys	C	
Glutamic acid	Glu	E	
Glutamine	Gln	Q	
Glycine	Gly	G	
Histidine	His	H	
Isoleucine	Ile	I	
Leucine	Leu	L	
Lysine	Lys	K	
Methionine	Met	M	
Phenylalanine	Phe	F	
Proline	Pro	P	

Amino acid name	Abbreviation	Single letter abbreviation	Structure
Serine	Ser	S	
Threonine	The	T	
Tryptophan	Trp	W	
Tyrosine	Tyr	Y	
Valine	Val	V	

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نظرة ثاقبة على العلاقة بين التركيب والنشاط لببتيد بريفينين المضاد للميكروبات

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ملخص

تم العثور على العديد من أنواع البرمائيات، وخاصة تلك من جنس رنا، لإنتاج الببتيدات المضادة للميكروبات الخطية، البرمائية، والكاتيونية .(AMPs)تكتسب AMPsمزيدًا من الاهتمام في الاستخدامات الصيدلانية نظرًا لطريقة عملها الرئيسية، والتي تستلزم اختراق وتمزيق أغشية الخلايا المقصودة بمقاومة منخفضة نسبيًا Brevinin .هي عائلة كبيرة من AMPsتمت دراستها على نطاق واسع خلال العقود القليلة الماضية. تحتوي العائلة بشكل أساسي على مجموعتين من الببتيدات، وهما Brevinin-1 و .Brevinin-2هذه الببتيدات كاتيونية وتؤسس هياكل ثانوية في بيئة الغشاء البيولوجي. نناقش آثار المعلمات الهيكلية)شحنة صافية، كارهة للماء، amphiphilicity، حلزونية، طول الببتيد، إلخ (لبريفينين على نشاطها المضاد للميكروبات. كقاعدة عامة، ستؤدي زيادة الشحنة الصافية إلى زيادة نشاط مضادات الميكروبات. ومع ذلك، فإن الشحنات الصافية المفرطة تزيد أيضًا من النشاط الانحلالي. تؤثر تركيبة الأحماض الأمينية بشكل كبير على الكراهية للماء والطائرة، والتي بدورها تؤثر على نشاط الببتيدات. المعلمات الهيكلية مترابطة أيضًا ؛ تغيير معلمة واحدة سيؤثر على الآخرين. سيعطي التغيير الأمثل في هذه العوامل نظير Brevinin أعلى نشاط مضاد للميكروبات ولكن أقل نشاط انحلالي.

الكلمات الدالة: الببتيدات المضادة للميكروبات ؛ بريفينين، لولبية، كره الماء، صافي الشحن النشاط الانحلالي.

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