Binding of Pediocin PA-1 with Anionic Lipid Induces Model Membrane Destabilization

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To obtain molecular insights into the action mode of antimicrobial activity of pediocin PA-1, the interactions between this bacteriocin and dimyristoylphosphatidylcholine (DMPC) or dimyristoylphosphatidylglycerol (DMPG) model membranes have been investigated in D2O at pD 6 by Fourier transform infrared spectroscopy. The interactions were monitored with respect to alteration of the secondary structure of pediocin, as registered by the amide I band, and phospholipid conformation, as revealed by the methylene ν(CH2) and carbonyl ν(C=O) stretching vibrations. The results show that no interaction between pediocin and DMPC occurs. By contrast, pediocin undergoes a structural reorganization in the presence of DMPG. Upon heating, pediocin self-aggregates, which is not observed for this pD in aqueous solution. The gel-to-crystalline phase transition of DMPG shifts to higher temperatures with a concomitant dehydration of the interfacial region. Our results indicate that pediocin is an extrinsic peptide and that its action mechanism may lie in a destabilization of the cell membrane.

Pediocin PA-1 is a 44-amino-acid (molecular mass, 4,629 Da; pl, 9.6) (35) class IIa bacteriocin (38) produced by Pediococcus acidilactici PAC 1.0 and naturally found in fermented sausages (37) or other meat and vegetable fermentations (5). Its sequence is highly homologous to other class IIa bacteriocins (59). The N-terminal 20-amino-acid half of pediocin is in the majority of cases polar or cationic and highly conserved, with the consensus sequence Y3-G4-N5-G6-V7. The C-terminal half (residues A21 to C44) is much less polar and less conserved, containing a hypothetical hydrophobic membrane interaction domain. Two disulfide bonds stabilize the peptide structure, the one between the residues 24 and 44 accounting for its broad range of antimicrobial activity (17). Because of its specific antimicrobial activity against the foodborne psychrotrophic pathogen Listeria monocytogenes, pediocin PA-1 can potentially serve as a nontoxic food preservative to improve the quality, naturalness, and safety (55) of dairy and meat products.

The data for Listeria innocua death induced by pediocin PA-1 reveal that its activity maximum is reached near pD 6 and decreases at pD 7 and 8 (15, 30). A relation between activity and structure alterations has not yet been completely established. The loss of activity as a function of pD seems to be associated to a structural reorganization and a decrease in the protein flexibility that in turn results in an irreversible aggregation upon heating (30). The C-terminal region is first involved in the aggregation process, resulting in a total inactivation of the protein (30). The N-terminal region participates in the aggregation process in a second step. Pediocin can exist in a soluble and hydrophobic structural form (16). In an aqueous environment, pediocin presents an unordered structure as seen by circular dichroism (75) and Fourier transform infrared (FTIR) spectroscopy (30), whereas upon adsorption to vesicles, a structural rearrangement occurs. It was inferred from circular dichroism data that the peptide forms a β-sheet domain in the presence of phospholipid membrane (75). Upon membrane binding, the N-terminal region is proposed to form a three-strand β sheet whereas the C-terminal half is thought to form an α-helix.

It has been inferred that the initial binding of pediocin to target cells occurs through electrostatic forces and involves the well-conserved cationic N-terminal half. A potential membrane receptor would participate in pediocin anchoring, but it is questioned whether it is absolutely required to mediate the peptide activity (22, 25). Membrane binding would be followed by the C-terminal half penetrating into the hydrophobic part of the target membrane, which would lead to membrane leakage (14). Then, some clues suggest that pediocin antimicrobial action consists of the formation of a pore within the cell membrane (17). However, the mechanism by which pediocin exerts its antimicrobial effect is not clearly established.

A way to provide insights into this research area is to study the interactions between pediocin and different phospholipids by using model membranes. This is especially relevant since dimyristoylphosphatidylglycerol (DMPG) constitutes an abundant part of Listeria membrane phospholipids whereas the dimyristoylphosphatidylcholine (DMPC) content increases at the expense of DMPG molecules in bacteriocin-resistant Lis-
acteria membrane (53, 74). As a consequence, to gain details into the mechanism by which pediocin PA-1 induces the cell death, we studied the interactions between pediocin PA-1 and DMPC or DMPG model membranes by using FTIR spectroscopy. This technique is known to be a versatile and powerful tool to investigate protein and lipid structure and their interactions. In particular, it allows the analysis of the hydrocarbon chain conformation (67, 68) and the interfacial region of the bilayers (28) as well as the determination of the secondary structure of protein in complex systems such as biological systems (46, 70) or functional states (45).

**MATERIALS AND METHODS**

**Sample preparation.** Pediocin PA-1 was purified from *P. acidilactici* PAC 1.0 (gift of Quest international, Sarasota, Fla.) culture supernatant as described previously (29). DMPG and DMPC were purchased from Avanti Polar Lipids (Alabaster, Ala.) and deuterium oxide (D$_2$O) from Sigma Chemical Co. (St. Louis, Mo.). All products were used without further purification.

The liposomes were made by hydrating lipid powder with phosphate-D$_2$O buffer (0.1 M, pD 6) at a concentration of 10% (wt/vol). Samples were vortexed above and below the main phase transition temperature ($T_m$) of the lipids. Three heating and cooling cycles were carried out. The pH was measured with a standard pH electrode, and the measured value was corrected according to the following formula: pD = pH + 0.4 (33).

Pediocin was first dissolved in phosphate-deuterium buffer (0.1 M, pD 6). Aliquots of pediocin solutions were then added to the liposome suspension, so that the pediocin-to-lipid ratio was 1:10 or 0.1:10 (wt/wt). At 20°C, the spectrum of pediocin in aqueous solution as a function of pD 6 (Fig. 1A) is broad, featureless, and centered at 1,645 cm$^{-1}$, which is typical of an unordered polypeptide chain (9a, 34, 71). For a peptide that is in a random coil conformation, each peptide bond experiences a multitude of dihedral angle values that account for the large bandwidth and the absence of almost any clear component in the deconvolved spectrum. However, the shoulder at 1,673 cm$^{-1}$ suggests the presence of some stable cations occur 0.1:10 (wt/wt) (Fig. 1B), strong structural modiﬁcation occurs.

**RESULTS**

Interaction between pediocin PA-1 and DMPG bilayers at pD 6. (i) Effect of DMPG on the amide I’ peptide vibration. Figure 1 presents the deconvolved amide I’ band of pediocin PA-1 at 1% (wt/vol) in pD 6 buffer as a function of temperature in the absence and presence of DMPG at 0.1:10 (wt/wt) and 1:10 (wt/wt) pediocin-to-lipid ratios. At 20°C, the spectrum of pediocin in aqueous solution at pD 6 (Fig. 1A) is broad, featureless, and centered at 1,645 cm$^{-1}$, which is typical of an unordered polypeptide chain (9a, 34, 71). For a peptide that is in a random coil conformation, each peptide bond experiences a multitude of dihedral angle values that account for the large bandwidth and the absence of almost any clear component in the deconvolved spectrum. However, the shoulder at 1,673 cm$^{-1}$ suggests the presence of some stable β-turns. The shoulder at 1,611 cm$^{-1}$ corresponds to amino acid side chain vibration. Upon heating up to 70°C, a small broadening and an increase in wave number are noticed. These are the usual thermal effects observed for vibration band wave numbers of chemical groups, suggesting that the secondary structure of pediocin is weakly affected by temperature in solution at pD 6, the peptide remaining essentially in a random coil conformation. Upon cooling to 20°C (data not presented), the spectrum after heating is identical to the spectrum before heating, which shows that the conformational changes are completely reversible.

In the presence of DMPG, for a pediocin-to-lipid ratio of 0.1:10 (wt/wt) (Fig. 1B), strong structural modifications occur...
with respect to the peptide in solution. At 20°C, the spectrum is still centered near 1,645 cm⁻¹ but it is less broad and presents discernible shoulders. This band narrowing as well as the emergence of distinctive band components upon interaction with the membrane can be ascribed to a reduction in the multitude of conformations adopted by the polypeptide chain in solution. This is likely to result from a membrane binding–induced conversion of the peptide from the random coil to a folded conformation. Such a structural reorganization can be, as proposed previously (30), associated to a decrease in the peptide flexibility. The assignment of the different components is classical and based upon the literature (34, 62). The major component at 1,645 cm⁻¹ may be assigned to undefined structures. However, a contribution from another structure such as 3₁₀ helices (type III β-turn) cannot be ruled out, since it is known to absorb approximately 1,639 to 1,642 cm⁻¹ in D₂O (54, 65) and is commonly found in peptides and globular proteins (20, 26). The shoulder located at 1,625 cm⁻¹ is attributed to β-strand, the one at 1,658 cm⁻¹ to α-helix, whereas the small components at 1,686 and 1,675 cm⁻¹ can be assigned to turns.

Heating from 20 to 50°C results in the broadening of the amide I band, which is characteristic of a peptide unfolding, although regular structural elements are still present (see the band at 1,686 cm⁻¹). At 60°C, two strong and narrow bands located at 1,618 cm⁻¹ and 1,630 cm⁻¹ appear. The first band corresponds to intermolecular β-sheets resulting from aggregation of proteins and peptides (11, 19, 45). However, the general profile of the amide I band is different from what is generally observed for aggregated proteins. In most cases, the bands located at 1,618 cm⁻¹ are accompanied by a band of approximately 1,680 cm⁻¹ in D₂O, which indicates that the β-sheets are antiparallel. They result from a splitting of the amide I mode induced by dipole transition coupling promoted by the close alignment of the polypeptide chains in antiparallel β-sheets (40). A spectral pattern similar to the one shown in Fig. 1B (obtained at 70°C) has already been observed with different peptides like uveopathogenic peptide (57), with magainin’s family peptide member in the presence of DMPG–cholesterol liposomes (36), and with pediocin in D₂O at pH 7 and 8 (30). These peptides present two major bands located near 1,613 and 1,627 cm⁻¹ in the aggregated state. The former was assigned to intermolecular hydrogen-bonded β-sheets, whereas the latter was related to β-sheet conformation (57) or to β-sheets involved in weak intermolecular hydrogen bonds (36). As seen in Fig. 1B, the two major bands increase concomitantly with temperature, suggesting that the vibrational band at 1,630 cm⁻¹ can also be associated with aggregation and in turn with the formation of intermolecular hydrogen bonds. Its wave number (1,630 cm⁻¹), higher than that assigned to intermolecular β-sheet (1,618 cm⁻¹), may indeed be related to weaker hydrogen bonds. Such a component is expected to occur for the aggregation of polypeptide chains that retain some secondary structure and prevent the close alignment of the chains (36). This is in agreement with the presence of the two components at 1,647 cm⁻¹ and 1,660 cm⁻¹ at 60°C, characteristic of residual native-like secondary structures.

Figure 1C presents the amide I band of pediocin for a peptide-to-lipid ratio of 1:10 (wt/wt) as a function of temperature. At 20°C, the spectrum of pediocin is close to the one shown in Fig. 1B. Since the amount of membrane-bound peptide may vary versus the peptide concentration, this absence of concentration effect indicates that all the peptides are bound to the membrane, suggesting a strong affinity of pediocin for DMPG. Upon increasing the temperature to 40°C, the spectrum presents two well-resolved components at 1,648 and 1,638 cm⁻¹, whereas the spectrum at 50°C is very close to that obtained for a lower pediocin content (Fig. 1B). Two bands at 1,618 and 1,632 cm⁻¹ appear at 60°C, and the spectrum in the aggregated state at 70°C is basically identical to that obtained above (Fig. 1B). These observations suggest that the unfolding pathways and the final aggregated states seem to be essentially the same for the two peptide concentrations.

(ii) Effect of DMPG on the tyrosine vibration. Pediocin PA-1 contains two tyrosine residues that are located near the extremity of the N-terminal group (Tyr2-Tyr3). The vibration of the tyrosine ring is known to absorb at around 1,515 cm⁻¹ (18, 73). The wave number is affected by the tyrosine local environment, being different according to whether it is exposed to water or to a hydrophobic environment. For example, it increases upon peptide unfolding (26, 61). Therefore, this vibration mode may represent a marker providing information relative to the N-terminal region of pediocin. Indeed, the tyrosine wave number of pure pediocin in D₂O evolved differently upon heating depending on pH, which showed that the N-terminal region can be (or not be) involved in the peptide aggregation (30). In Fig. 2 is plotted the wave number of the tyrosine residues as a function of temperature in the absence and presence of DMPG for the two pediocin-to-lipid ratios. In each case, there is no significant variation of the wave number with increasing temperature, suggesting no change in the microenvironment of the tyrosine residues. The wave number is nearly constant at ~1,516 cm⁻¹ for the protein alone, whereas it is ~1514.5 or ~1513.5 cm⁻¹ for a peptide-to-lipid ratio of 0.1:10 or 1:10 (wt/wt), respectively. This decrease in the tyrosine wave number upon membrane binding can be related to a more hydrophobic environment in the vicinity of the N-terminal part, either induced by the peptide folding or by the close
proximity of hydrophobic lipid groups near the N-terminal region.

(ii) Effect of pediocin PA-1 on the CH$_2$ stretching vibration of DMPG. The impact of pediocin on DMPG bilayers was investigated. The C-H stretching vibration of the lipid chains was studied first. Two main bands around 2,918 and 2,850 cm$^{-1}$ dominate the spectra in this region (spectra not shown). They are assigned to the antisymmetric [v$_{as}$(CH$_2$)] and symmetric [v$_{s}$(CH$_2$)] methylene stretching mode, respectively. The thermotropism of lipids is characterized by the shift of the wave number of these modes that has been shown to be sensitive to the presence of gauche conformers (1, 10, 12). Thus, they are useful probes for monitoring lipid phase transitions (49, 72). However, other effects such as intermolecular coupling and librotorsional mobility can also influence the v$_{s}$(CH$_2$) and v$_{as}$(CH$_2$) wave numbers (39, 43, 58, 63). Figure 3 presents the evolution of the v$_{s}$(CH$_2$) wave number of DMPG acyl chains as a function of temperature in the absence and presence of pediocin. For pure DMPG, the transition temperature T$_{m}$ is 23°C, as deduced from the midpoint of the curve, which is in agreement with the literature (76). For a peptide-to-lipid ratio of 0.1:10, T$_{m}$ is almost unaffected by the presence of pediocin. The wave number of the v$_{s}$(CH$_2$) mode in the gel and liquid-crystalline phases is unchanged, indicating that pediocin does not alter the conformation of the acyl chains. For a peptide-to-lipid ratio of 1:10, T$_{m}$ shifts from 23 to 33°C, suggesting that pediocin strongly stabilizes the gel phase. A similar phenomenon was observed for nisin (7). It is very likely that at the lowest peptide concentration (0.1:10), a too small amount of lipids is affected for the stabilizing effect to be detected. Furthermore, there is no impact on the v$_{s}$(CH$_2$) wave number in both phases whatever the peptide concentration, indicating that pediocin does not interact with the lipid chains and then suggesting that no portion of the peptide inserts within the hydrophobic core of the bilayers.

(iii) Effect of pediocin PA-1 on the ester C=O vibration of DMPG. The stretching vibration of the lipid carbonyl groups [v(C=O)] can provide details concerning the hydration, the environment, and the conformation of the membrane interfacial region. The ester band of DMPG is known to be composed of two overlapped components located near 1,742 and 1,727 cm$^{-1}$, which can be evidenced by FSD. The former and latter bands are attributed to free (anhydrous) and hydrogen-bonded (hydrated) carbonyl groups, respectively, but the conformation of the glycerol backbone may also influence the v(C=O) band (6, 32, 48). Thus, the study of this band as a function of temperature provides insights into the hydration level of the polar-apolar interface of DMPG bilayers. Figure 4 presents such an analysis for DMPG bilayers in the absence (Fig. 4A) and presence (Fig. 4B and C) of pediocin. Without pediocin (Fig. 4A), there is a well-known intensity increase in the low-wave-number component upon increasing temperature, interpreted as a rise in the amount of water molecules bound to the ester groups due to a higher penetration of water into the interfacial region above the phase transition. For a pediocin-to-lipid ratio of 0.1:10 (Fig. 4B), the thermal behavior of the v(C=O) band is basically the same as that observed in the absence of pediocin. This result is consistent with the absence of pediocin effect on the v$_{s}$(CH$_2$) wave number at this concentration. For a peptide-to-lipid ratio of 1:10 (wt/wt), the beginning of the thermal behavior of the C=O groups between 10 and 20°C is close to that observed above. Between 23°C (i.e., the T$_{m}$ of pure DMPG) and 33°C (the transition temperature of DMPG in the presence of pediocin), there is a dramatic narrowing and a shift of $\sim$3 cm$^{-1}$ of the v(C=O) bands. Similar observations already were observed for DMPG and phosphatidylserine bilayers upon addition of divalent cations (13, 21, 28) or upon incubation at 2 to 4°C of saturated phosphatidylcholine and phosphatidylglycerol bilayers, which results in the formation of the so-called subgel phase (47). Such spectral features were attributed to immobilized and dehydrated carbonyl groups due to an isothermal crystallization of the phospholipid molecules. A low wave number of the v$_{s}$(CH$_2$) band (approximately 2,849 to 2,850 cm$^{-1}$) accompanied these changes, which is characteristic of ordered chains. This finding is also found to be true here, since, as seen in Fig. 3, in the temperature range of 23 to 33°C the v$_{s}$(CH$_2$) wave
number is characteristic of the ordered chains of the gel phase. Therefore, the results can be rationalized by considering an effect of this peptide on DMPG similar to that of divalent cations or incubation at low temperatures. It is likely that upon cooling the samples to a temperature below the chain-melting $T_m$ for our thermal studies, pediocin also induces a progressive crystallization of the phospholipids. In fact, the nucleation of this solid-like phase occurs at low temperature. However, the growth of this phase is slow at these temperatures but increases upon heating, which explains why immobilized $\text{H}^9\text{O}$ groups are evidenced near the gel-to-liquid crystalline phase transition. When the sample is further heated, the liquid crystalline phase is reached. This phenomenon is widespread and has already been found with oleoyl-palmitoyl phosphatidylcholine (44).

Interaction between pediocin PA-1 and DMPC bilayers at pD 6. The interactions between pediocin and the zwitterionic phospholipid DMPC in pD 6 buffer as a function of pediocin concentration have also been studied as above. The results (data not shown) indicate that, on one hand, the amide I band of pediocin is not modified in the presence of DMPC with respect to that of pediocin in solution and, on the other hand, neither the methylene stretching modes of the acyl chains nor the $\nu(\text{C}==\text{O})$ band is affected by the presence of the peptide with respect to the pure lipid. In addition, the thermal behavior of the phospholipid vibration bands is unchanged with respect to those observed in the absence of pediocin, whereas the amide I band recorded as a function of temperature is the same as that of pediocin in aqueous solution. As a consequence, it seems that pediocin has little or no affinity for DMPC, whatever the concentration used in the present study.

DISCUSSION

Pediocin PA-1 does not interact with the zwitterionic lipid DMPC but does interact with DMPG, suggesting no affinity of this peptide for neutral lipids. Significant modifications have been found for the pediocin-DMPG system, but the influence of pediocin on the lipids requires a minimal concentration to be detected. Pediocin binds to membranes made with anionic lipids, suggesting that a negatively charged membrane or negatively charged domains, which result from lipid heterogeneities within the membrane, can alone drive the binding of pediocin through electrostatic interactions. Indeed, pediocin PA-1 has a net charge of $+8$ and DMPG has a charge of $-1$ at pH 6 (15, 16). It may be inferred that the membrane binding of pediocin does not necessarily require a specific receptor, although a contribution of such a molecule cannot be completely ruled out.

The spectrum of pediocin in the amide I region reveals an important conformational reorganization upon binding to DMPG compared to the peptide in aqueous solution. This provides a direct proof that pediocin PA-1 can exist under two structural forms, which is in agreement with the literature (14). The former form corresponds to a random coil adopted in D$_2$O buffer at pD 6, whereas the latter is characterized by a more structured conformation. The spectrum of bound pediocin at 20°C indicates the presence of undefined segments and/or type III $\beta$-turns. It seems that $\alpha$-helix, $\beta$-strand, and turns are also present. These observations are in agreement with those of Watson and collaborators (75), who showed that in the presence of vesicles made up with phospholipids from Listeria innocua Lin11, pediocin is constituted of unordered structures (32%), $\alpha$-helices (32%), $\beta$-strands (17%), and turns (19%).

At pD 6, the peptide in aqueous solution undergoes small and reversible structural modifications upon heating up to 80°C and remains essentially in a random conformation, showing that pediocin is thermostable up to 80°C. As seen previously (30), the conformation of pediocin is more structured at a pD above 6. The more-folded conformation is favored, since
an increase in the intramolecular electrostatic repulsions generally destabilizes the peptide structure (2, 56). In particular, this may result from changes in the protonation of the three histidine residues (His12, His38, and His42) upon raising the pD above 6. The heat-induced denaturation of bound pediocin leads to an irreversible self-aggregation that is more extensive as the pD increases from 7 to 8 due to the decrease in the intermolecular electrostatic repulsions (77). In the presence of DMPG at pD 6, the thermal behavior of pediocin is different from that observed for the peptide alone. Pediocin unfolds upon heating and irreversibly aggregates above 60°C. Then, the restructuration at 20°C and the subsequent heat-induced aggregation of pediocin in the presence of the negatively charged membrane are similar to what is observed in aqueous solution at a pD above 6. This can be ascribed to direct interactions between positively charged amino acid residues and negatively charged phospholipid head groups or to a (partial) charge neutralization of the peptide that allows the peptide to fold into a more compact and structured conformation. The important role played by the hydrocarbon-water interface on the structure of pediocin has already been noted (75). The membrane effect can be due to electrostatic interactions, as suggested above, but it can also arise from the reduction of the number of degrees of freedom of the peptide and thus to the observed formation of secondary structures (66). Finally, once bound to the interface, the peptide density at the membrane surface is much higher than the density in the bulk, which favors peptide-peptide interactions and then promotes the observed self-aggregation.

It is noteworthy that during the thermal treatment there is no significant change in the environment of the two tyrosine residues of DMPG-bound pediocin. Since they are localized in the N-terminal end of the peptide, this result indicates that the N-terminal region is not sensitive to the unfolding and aggregation. As a consequence, it seems that during heating this region always remains in a constant environment that could be provided by the membrane. If such is the case, the N-terminal end could directly be involved in the anchoring of pediocin to the membrane. However, the data of the tyrosine vibration can also be rationalized by considering that the N-terminal region could keep the same configuration, thus providing the same environment to the tyrosine residue.

Regarding the effect of pediocin on model membranes, we found no modification of the ν(CH3) value of DMPG in the gel and liquid-crystalline phases, suggesting no direct perturbation of the lipid acyl chains and no insertion within the bilayer hydrophobic core. However, the observed increase in Tm can confidently be related to an extrinsic behavior of pediocin. This conclusion is also in agreement with the data obtained for the ν(C=O) region, suggesting a strong dehydration and immobilization of the carbonyl groups as a result of the presence of the peptide molecules at the membrane interface. As a consequence, we may suppose that all the changes seen in the pediocin structure result from interfacial interactions. Other proteins have been found to behave as an extrinsic protein with DMPG, like gramicidin (8) and nisin (23). The latter is also a bacteriocin (type 1) and has been found to interact mainly at the membrane interface with limited contacts with the hydrophobic core of the bilayer.

Many hypotheses have been proposed to explain the mechanism of pediocin activity. The more generally admitted explanation involves the insertion of the C-terminal part of the peptide into the membrane, which induces pore formation and then cell death. Nevertheless, the potential interfacial interaction of a hinge structural element of pediocin (4) and the capacity of the C-terminal part to participate in the target cell recognition and then ensuring the bacteriocin specificity (27) both suggest that another mechanism could exist. Moreover, the increase in Tm, the ν(C=O) alteration, and the extrinsic behavior of pediocin are not consistent with the pore mechanism. They rather suggest a destabilization of the membrane, a subsequent permeation, and finally the cell death. A controversy similar to the one over the pore mechanism has been raised over other antibacterial proteins or peptides like nisin (9, 23, 24), dermaseptin (64, 69), ececrin (31), magainin (50, 51), diasteroisomers of melittin (60), and melitin (3, 41, 42, 52). The interfacial destabilization of the membrane by the peptide and the subsequent cell death seem to be common features. It was suggested that such a membrane permeation may occur through a carpet-like structure (60, 69).

To conclude, this study reports the effects of pediocin PA-1 on model membranes. We show that the association with the membrane interface of DMPG does affect the conformation of the peptide, the adsorption inducing a more folded structure. This association may be induced by electrostatic interactions between the peptide and the negatively charged membrane. These interactions do not require the presence of a receptor. Nevertheless, the presence of a receptor should promote the access to the surface of bacterial membranes. If such a receptor exists, it could be recognized by the C-terminal part of the peptide that has been shown to be a determinant factor for target cell specificity (27). Pediocin PA-1 seems to be located at the surface of anionic membranes and induces a dehydration of the interfacial region. This peptide location could in turn result in the membrane leakiness and finally in cell death.

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