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Research Article 研究报告

益生菌治疗宠物细菌性腹泻概述

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摘要：益生菌是一类对宿主健康有益的活体微生物，在预防、治疗和修复宠物细菌性腹泻等疾病中引起人们广泛关注。抗菌药在治疗宠物细菌性腹泻中发挥了重要作用，随着细菌耐药性加剧，严重降低了抗菌药的治疗效果。益生菌治疗细菌性腹泻具有广阔的应用前景。本文概述了宠物腹泻的致病菌种类、腹泻特征及防治现状，同时对改善宠物胃肠道疾病相关的益生菌种类、筛选条件、作用机制、存在问题及应用前景进行了介绍。

关键词：宠物，细菌性腹泻，益生菌

近年来，随着我国经济的不断发展及人们精神生活水平的提高，宠物市场呈现蓬勃发展的趋势。在我国，城镇平均养宠率预计到 2021 年将升至 19%，犬和猫的总占比可达 80%[1]。根据《2019 年中国宠物行业白皮书》显示，国内宠物消费市场规模已高达 2024 亿元，其中宠物药品消费增速最快。胃肠道疾病是宠物的常发病之一，腹泻是胃肠道疾病最常见的临床症状[2]。流行病学调查显示在患胃肠道疾病的犬猫当中，有腹泻症状的分别占 35.9% 和 43.0%[3]，并且犬猫腹泻率最高可占所有宠物腹泻的 93.5%[4]。致病菌是导致宠物腹泻的主要原因之一[5–6]，通过致病菌分泌细菌毒素而引起肠道上皮稳态紊乱。导致宠物腹泻的致病菌有很多，包括弯曲杆菌[7]、肠致病性大肠杆菌[8]、沙门菌[9]和艰难梭菌[10]等。目前的主要治疗手段是使用抗菌药，但由于抗菌药的不合理应用，使宠物及其与人类接触的环境中均出现了耐药菌[11]，降低其治疗效果。此外，宠物有可能成为耐药基因的储存库[12]，成为兽医及公共卫生安全的重要问题。与此同时，其他治疗方法如疫苗及噬菌体在宠物上尚未有产品上市，而益生菌在治疗细菌性腹泻方面具有良好效果[13]。因此，探讨益生菌在治疗宠物细菌性腹泻中的应用具有重要意义，以期为宠物专用益生菌的开发和合理使用提供参考。

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1 宠物细菌性腹泻

1.1 宠物细菌性腹泻的致病菌

肠道上皮细胞对离子和溶质吸收及分泌的失衡会使机体丧失过多体液及电解质，进而表现腹泻症状，严重时甚至会导致死亡。引起犬猫腹泻的原因有多种，其中主要包括过敏、理化因素、细菌、病毒及寄生虫等。细菌性腹泻影响广、危害大且发病率高，通常是宠物食用腐败、不洁等细菌污染的食物造成的。致病菌的种类较多，本文总结了引起犬猫腹泻的常见致病菌及其所占比例。由表 1 可知，弯曲杆菌、肠致病性大肠杆菌、沙门菌、产气荚膜杆菌及艰难梭状芽孢杆菌是导致犬猫腹泻的主要致病菌。同时，我们发现不同国家及地区导致腹泻的病原菌及占比各不相同，当然这可能也与宠物的种类、年龄、生活环境、伴随疾病或其他肠道致病菌的混合感染有关。

1.2 宠物细菌性腹泻的特征

宠物细菌性腹泻通常是急性的，在幼年犬猫(1 岁龄内)中最为常见[4]，严重程度从轻度自限性腹泻到致命的急性出血性腹泻不等[21]，多发于夏秋两季，每年在 8 月至 9 月达到高峰[24]。成年犬的腹泻率高于成年猫，但幼年犬猫的腹泻率无差异[4]。细菌性腹泻会引起宠物正常肠道菌群组成[25]、多样性及代谢的改变[26–27]，破坏胃肠道稳态。临床特征表现为反复腹泻、呕吐、腹痛、里急外重、胀气和脱水等，有些猫会发展成大便失禁、肛周肿胀和皮炎。宠物发病初期，粪便为水样，往往还伴随着体温的升高，食欲及精神状态一般变化不大，而到中后期体温会恢复正常或下降，粪便呈黏液状。若长期未治愈则出现进行性消瘦，严重者发展成胃肠炎或脑炎，如不及时治疗，死亡率可达 90%。

表 1. 常见致病菌种类及其在腹泻犬猫中所占的比例
Table 1. The species and distribution of common bacterial pathogens in dogs and cats with diarrhea

Species	Dog	Country	Cat	Country
Campylobacter	60%[14]	Ireland	31%[15]	Italia
	97%[16]	Canada	16%[17]	Norway
Escherichia coli	35.1%[18]	United Kingdom	42%[19]	America
Salmonella	55%[20]	United Kingdom	68.9%[20]	United Kingdom
Clostridium perfringens	45.2%[21]	America	50%[22]	America
Clostridium difficile	18%[21]	America	3.7%[23]	Germany

1.3 宠物细菌性腹泻的防治现状

程度轻微的细菌性腹泻，一般可以通过饮食控制来自我恢复。严重感染的宠物通常需要进一步的评估，如粪便涂片镜检和细菌分离培养。在完成致病菌的分离鉴定后，通常选择性使用抗菌药进行治疗，从短期来看，抗菌药具有较好的治疗效果，但停药后腹泻往往会复发，特别是使用广谱的抗菌药，出现抗菌药相关性腹泻(antibiotic-associated diarrhea，AAD)。

在宠物门诊，除了明显由寄生虫引起的腹泻，一般都使用抗菌药进行治疗[28]，不合理或大剂量地使用抗菌药带来诸多问题：耐药菌出现、破坏肠道正常微生物群、诱发抗菌药相关腹泻。一方面，耐药菌的出现会导致宠物临床疾病治疗失败；另一方面，由于宠物与人类的密切接触，可能会将耐药菌传给人类，危害公共卫生安全[29]。人们一直在寻找抗菌药的替代治疗方案。接种疫苗是预防及控制细菌性腹泻的经济有效的手段，然而目前尚无应用于宠物的疫苗上市。益生菌长期以来一直作为宠物腹泻的治疗或补充治疗制剂[30]，根据不同属、物种、菌株和剂量的微生物的试验

组合分析得出，许多益生菌可以缩短急性腹泻的持续时间[31]。益生菌可能主要通过抑制或杀死致病菌，增加肠道有益菌，进而改善了宠物的腹泻状况。研究表明腹泻犬喂食含有 3 种犬源益生菌(发酵乳杆菌 VET 9A、鼠李糖乳杆菌 VET 16A、植物乳杆菌 VET 14A)的酸奶，可改善犬的食欲、腹泻状况，减少呕吐次数，降低腹泻犬粪便中致病菌的数量[32]。同样，给猫喂食粪肠球菌 SF68 后，可以维持猫肠道的微生物多样性，明显缓解腹泻症状[33]。此外，健康犬饲喂乳酸杆菌，也可以显著降低有害菌数量，增加有益菌数量[34]。例如，在英国随着 2014 年至 2018 年间益生菌制剂应用比例不断增加，批准用于小动物胃肠道疾病(口服和注射剂型)的抗菌药比例相应降低[4]。目前，国内宠物益生菌制剂尚处于起步阶段，专门用于治疗宠物腹泻的益生菌制剂还较少。

2 益生菌

2.1 益生菌的种类

微生物的益生特性与宿主特异性有关[35]。因此，益生菌的种类应来源于宿主肠道。目前，大多数应用于犬猫的益生菌并不源于它们胃肠道微生物群，但犬猫的肠道富含具有益生菌潜力的微生物[36]，至今也很少有关于宠物源益生菌产品的研究发表。目前，只有 6 种菌株被欧洲食品安全局认定为对小动物安全有效的益生菌，其中包括屎肠球菌(NCIMB 10415) 4b1705 和(NCIMB 10415) 4b1707，嗜酸乳酸杆菌(DSM 13241 25)和(D2/CSL) 4b1715，动物双歧杆菌，以及枯草芽孢杆菌(C3102) 4b1820[37–39]。

我国农业部批准用于饲料添加剂的益生菌有 34 种，其中多为乳酸菌，其次是芽孢杆菌和酵母菌。但是我国关于小动物益生菌的使用尚无明确规定，目前往往比照大动物标准。因此本文调查了我国部分品牌宠物益生菌制剂的菌种。如表 2 所示，嗜酸乳杆菌、植物乳杆菌、双歧杆菌、粪肠球菌、屎肠球菌、枯草芽孢杆菌、地衣芽孢杆菌和凝结芽孢杆菌的应用较普遍，剂型包括粉末、片状、胶囊及膏状等，可以满足不同的给药途径，含 2 种以上的复合菌粉末制剂为主流。同时我们发现各产品包装上标识的活菌数量均大于 10^7 CFU/g，但其能否耐受机体环境而存活是未知的，因此在筛选益生菌时就应作出相关的要求及标准。

2.2 益生菌的筛选条件

益生菌制剂成败的关键在于菌种的研究与筛选。益生菌制剂虽已广泛应用于宠物，但目前的动物用益生菌质量控制较差，宠物源益生菌亟待筛选与开发。益生菌的筛选需要一个系统的、循序渐进的方法，如图 1 所示，经过这一流程，最终筛选出具有功能特性且没有任何负面作用的安全菌株。

2.2.1 宿主相关抗应激能力：活的益生菌才能发挥作用[40]，所以在宿主体内益生菌需要具有一定抗应激能力。在口腔中，益生菌能够抵抗唾液淀粉酶和溶菌酶的作用。进入胃肠道后，需耐受低 pH 值、胃液、胃蛋白酶、胰液和胆汁盐，以及宠物的体内温度。pH 2–5 和 0.3%–2.0%的胆盐常作为筛选益生菌的标准之一[41]，如乳酸菌普遍耐酸，而双歧杆菌对低 pH 极为敏感，在 pH 2 和 pH 3 时存活率低或为 0[42]。此外，胞内海藻糖的积累与细菌耐热性相关，可以用来判断益生菌的高温耐受性[43]。从宠物肠道中分离筛选的益生菌，在胃肠道的存活率可能更高。

表 2. 我国部分宠物益生菌制剂包装上标识的菌种及活菌数

Table 2. The claimed species and viable counts of bacteria of probiotic preparations for companion animals in China

Types	Brand (Trade name)	Dosage form	Species	Viable count (Label)/(CFU/g)
Single probiotic preparation	Nourse (Multivitamin tablet for cat)	Tablet	*Bacillus subtilis*	$\geqslant 2\times10^{10}$
	Qingyulaodi (Probiotic tablets)	Tablet	*Bacillus subtilis*	No description
	Ramical (Calcium & intestine double effect tablets)	Tablet	*Bacillus subtilis*	$\geqslant 2\times10^{11}$
Combined probiotic preparation	Chongerxiang (G-pet probiotic powder)	Powder	*Lactobacillus acidophilus*	$\geqslant 5\times10^{7}$
			Enterococcus faecalis	$\geqslant 5\times10^{7}$
			Bifidobacterium longum	$\geqslant 5\times10^{7}$
	Xiaochong (Enterogastric guard)	Powder	*Bacillus subtilis*	$\geqslant 2\times10^{10}$
			Bacillus licheniformis	$\geqslant 1\times10^{10}$
	Crazydog (Pets nutritious lactobacillus supplement)	Powder	*lactobacillus plantarum*	$\geqslant 1\times10^{9}$
			Enterococcus faecium	$\geqslant 1\times10^{9}$
			Lactobacillus acidophilus	$\geqslant 1\times10^{8}$
			Bacillus coagulans	$\geqslant 1\times10^{8}$
	Climca (Probiotic)	Powder	*lactobacillus plantarum*	$\geqslant 6\times10^{8}$
			Bacillus subtilis	$\geqslant 1\times10^{9}$
			Bacillus coagulan	$\geqslant 4\times10^{8}$
			Bacillus licheniformis	$\geqslant 1\times10^{9}$
	Keres (Nutritional supplement for pet)	Powder	*Bacillus licheniformis*	$\geqslant 1\times10^{9}$
			Bacillus subtilis	$\geqslant 1\times10^{9}$
			Lactobacillus acidophilus	$\geqslant 1\times10^{8}$
			Bifidobacterium animalis	$\geqslant 1\times10^{8}$
	Golden (Enterogastric guard)	Powder	*Bacillus subtilis*	$\geqslant 3.2\times10^{9}$
			Enterococcus faecalis	$\geqslant 3.2\times10^{9}$
			lactobacillus plantarum	$\geqslant 8\times10^{8}$
	Pet food (Nutrient for intestine)	Tablet	*Lactobacillus Active ferment*	$\geqslant 7\times10^{8}$
	Vetpet (Probiotics for cat)	Paste	*Multiple lactobacillus*	$\geqslant 1\times10^{9}$
	Balance (Pet probiotic)	Paste	*Bacillus subtilis*	$\geqslant 8\times10^{8}$
			Lactobacillus acidophilus	$\geqslant 2.8\times10^{8}$
			Enterococcus faecalis	$\geqslant 4.2\times10^{8}$
			Streptococcus thermophilus	$\geqslant 2\times10^{8}$

2.2.2 上皮黏附能力：只有定殖于肠道上皮细胞足够时间，益生菌才能发挥作用[44]。益生菌能够黏附在肠上皮细胞取决于两个膜(益生菌细胞膜和上皮细胞膜)的复杂接触过程，细菌胞外成分及周围组成也会影响其黏附[45–46]。除了可以直接利用哺乳动物细胞系来测定益生菌的黏附能力，还可以通过测定益生菌的自聚力及细胞表面疏水性来判断其黏附性。益生菌的自聚力可以使其在肠道中集聚到足够的细菌浓度，而细胞疏水性则提高了细菌与上皮细胞的相互作用。用磷酸盐缓冲液(PBS)测定益生菌株悬液在不同时间的吸光度，即可判断益生菌的自聚力[47]。细胞表面疏水性则可以通过 MATH (Microbial adhesion to hydrocarbons，MATH)的方法测量[48–49]。

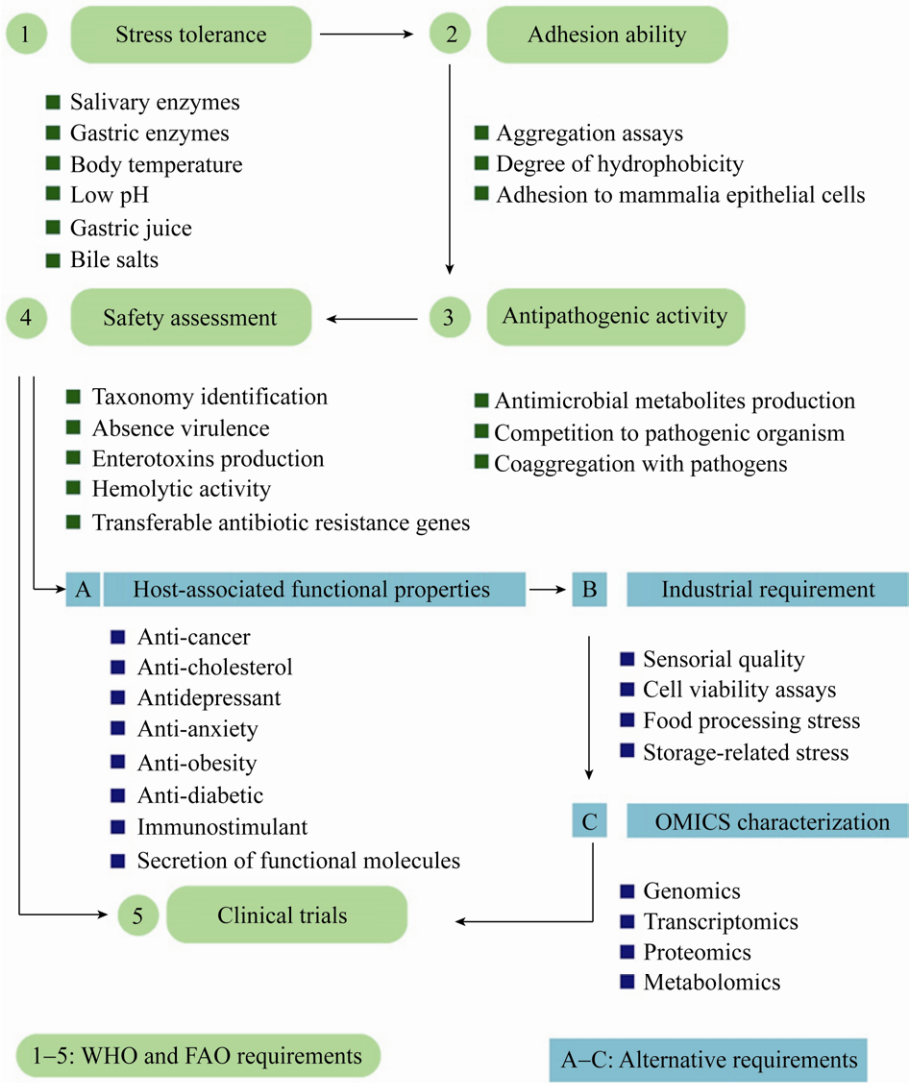

图 1.　筛选鉴定益生菌菌株的方法[52]

Figure 1.　Methods of screening and identification of probiotics[52].

2.2.3　抗菌效果：益生菌一旦定殖在肠道，可以通过多种作用机制发挥抗菌效果。益生菌产生某些代谢产物能够直接抑制或杀死致病菌，该特性可以通过琼脂平板的抑菌圈法测定[50]。益生菌与致病菌的共聚合作用可以抑制致病菌在肠道中的定殖，这一特性可以根据益生菌与不同致病菌的共聚合试验来评价。

2.2.4　安全性：宠物摄入的益生菌不一定是完全安全的，若不测定其安全性，可能益生菌给宠物带来的危害远远大于其益生作用。益生菌安全性的评定主要是进行菌种鉴定，并检测益生菌是否具有溶血性、毒力因子和可转移耐药基因[51]。益生菌种可通过生化试验、16S rRNA 测序、质谱法等方法进行鉴定。益生菌溶血性可以通过血平板培养判断。目前，细菌毒力和可转移耐药基因的鉴定则主要是通过全基因组测序分析。

2.2.5　临床试验：通过体外和动物试验研究后，还需经过临床试验来验证益生菌安全性和有效

性。在进行临床试验时，应采用合理的科学原则，如要确定研究的宠物种类、设置对照组和有足够的样本量。同时，还要考虑益生菌的给药途径，如通过口服、直肠或阴道途径给药。

以上总结是益生菌成为候选株的基本条件，以期为我国制定宠物用益生菌筛选的相关法规提供参考。益生菌的宿主相关功能特点(抗病毒、抗氧化、抗焦虑等)，工业生产要求以及生物组学特性为选择性要求。

2.3 益生菌的作用机制

益生菌能够帮助宠物抵御致病菌并缓解细菌性腹泻的研究已较为明确，但其作用机制有多种且较为复杂，因此本文归纳总结了目前益生菌作用机制的研究进展情况。如图 2 所示，益生菌防止致病菌对胃肠道造成损害的作用机制主要分为 3 大类，分别是直接拮抗、免疫调节和排斥作用。

2.3.1 拮抗作用：益生菌通过杀死或抑制致病菌以限制感染，或下调致病所需的黏附素或毒素等毒力因子的表达来发挥拮抗作用。

(1) 分泌具有抗菌活性的小分子或生物活性肽。金黄色葡萄球菌通常在肠道中定殖，是无害的，但在皮肤屏障或免疫系统受损时，则会导致

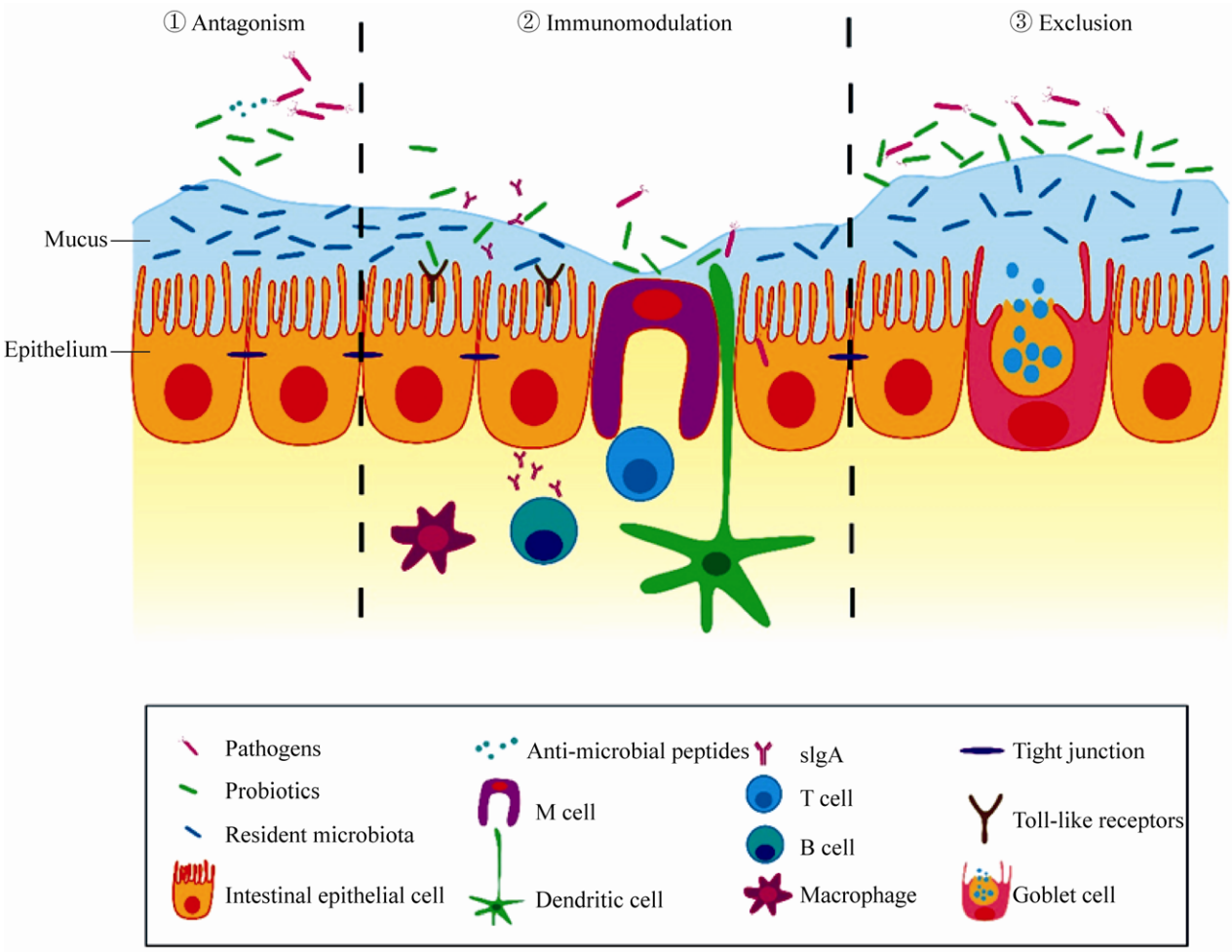

图 2. 益生菌抑制致病菌感染肠道的三种机制

Figure 2. Three mechanisms of probiotics on protecting intestine from pathogenic bacteria infection.

严重的感染。研究发现，枯草芽孢杆菌 CAU21 的次级代谢产物优化得到的 bacaucin-1 对金黄色葡萄球菌及耐甲氧西林金黄色葡萄球菌(methicillin-resistant *S. aureus*，MRSA)具有特异性的杀菌作用[53]，这为益生菌降低 MRSA 感染率提供有效依据，也为化学和机理多样性的非核糖体抗菌肽(NRAP)用于新型抗菌药的开发奠定基础[54]。另外，乳酸菌是益生菌制剂中的第一大菌属，一些乳酸杆菌在生长过程中也可以产生天然的抗菌物质，从而抑制致病菌的生长繁殖[55]，如唾液乳酸杆菌 UCC118 可以通过产生细菌素 Abp 118 保护小鼠免受李斯特菌的感染[56]。因此，许多益生菌可通过产生抗菌分子直接抑制或杀灭肠道中的致病菌，使宿主免受疾病损害。

(2) 影响致病菌群体感应系统/抑制致病菌的毒力基因或蛋白表达。有研究指出，每天喂食小鼠产芬芳素(fengycin)的枯草芽孢杆菌可以影响 MRSA 的群体感应，进而阻止 MRSA 在肠道中定殖[57]，这是首批准确描述益生菌如何提供健康益处的研究之一。另外，嗜酸乳杆菌可抑制群体感应系统的 2 型自诱导信号分子(autoinducer-2，AI-2)而降低肠出血性大肠杆菌 O157:H7 毒力因子的表达[58]，罗伊氏乳杆菌 RC-14 也是通过影响群体感应而降低金黄色葡萄球菌中毒休克综合征毒素-1 的表达[59]。因此，益生菌可以通过影响群体感应或降低致病菌的毒性，间接减少致病菌对肠道的损害。

2.3.2 免疫调节作用：益生菌与宿主免疫系统相互作用，从而提高机体的免疫力以抵御致病菌。参与免疫相互作用的益生菌效应分子，包括细菌细胞壁成分以及特定的蛋白质。商业应用的益生菌大多为革兰氏阳性菌，其细胞壁较厚，由多层肽聚糖、包膜多糖、脂蛋白和脂磷壁酸组成。其中一些分子包含微生物相关分子模式(microbe-associated molecular pattern，MAMPs)，可以被宿主肠道黏膜的特定模式识别受体(pattern recognition receptors，PRRs)识别[60]，从而诱导免疫细胞反应及调节细胞因子的分泌。

(1) 诱导免疫细胞产生多种反应。益生菌不仅可以被树突状细胞识别，使它们细胞膜表面的 Toll 样受体 2 (Toll-like receptor 2，TLR2)以及甘露糖(CD206)表达增加[7]，还可以与微褶细胞(M 细胞)结合，进行免疫调节[61]。乳酸菌还可以诱导调节性 T 细胞，上调转化生长因子-β (TGF-β)[62]。最终，机体的免疫系统被调动来抵抗致病菌的入侵。

(2) 调节 sIgA 及细胞因子的分泌。乳酸菌的脂磷壁酸(lipoteichoic acid，LTA)可以通过 TLR2 刺激宿主促炎因子 TNF-α 的分泌[63]，嗜酸乳杆菌 A4 可上调肠道中促炎因子 IL-8、IL-1β 和 TNF-α 水平[64]。相对于乳酸菌的促炎活性，长双歧杆菌 BIF53 可促进抑炎因子 IL-10 的产生[65]。肠腔 sIgA 含量的增加同样可调节机体免疫应答，如动物双歧杆菌 Bb-12 可诱导肠道中 IgA 的分泌[66]。所以，益生菌诱导免疫细胞产生细胞因子，进而发挥其调节免疫、细胞生长及损伤组织修复等功能。

2.3.3 排斥作用：益生菌与致病菌竞争结合位点或改变肠道微环境、调节肠道菌群、改善肠道屏障功能，从而限制致病菌附着、进入或易位。

(1) 与致病菌竞争结合位点。益生菌的竞争性排斥是基于细菌与细菌之间的相互作用，这种相互作用是由对可利用营养物质和细菌黏附位点的竞争介导的。某些益生菌菌株可利用表面蛋白与黏液相互作用，通过其特有的黏附特性阻碍致病

菌的定殖[67]。还有一些益生菌可以通过分泌蛋白降解碳水化合物受体，产生受体类似物和生物表面活性剂来抑制病原体黏附[68]。而对于乳酸菌和双歧杆菌，它们同致病菌一样有与碳水化合物结合的特性，因此可以直接与致病菌竞争宿主细胞受体[69–71]。益生菌的存在使致病菌无法定殖于肠道上皮细胞，从而使肠道免受损害。

(2) 调节肠道微环境。益生菌往往能够产生酸性物质降低肠道内的 pH 值，如双歧杆菌能够在肠道产生醋酸，进而通过酸相关机制抑制志贺产毒大肠杆菌[72]，犬粮中添加益生菌后，粪便中乙酸、丙酸、丁酸的含量明显增加，肠道中形成的酸性环境抑制了致病菌的入侵[73]。

(3) 调节肠道菌群。目前已经发现犬猫肠道中含有 10 种以上的细菌门，其中厚壁菌门、拟杆菌门、变形杆菌门、梭杆菌门和放线菌门占 99%以上[74]。正常肠道共生菌是抵御病原体入侵的屏障之一，益生菌可以通过调节犬猫肠道中的微生物组成而保护肠道健康，如猫服用了商用益生菌粪肠球菌 SF68 可以维持肠道中的微生物多样性，从而腹泻症状得到明显缓解[33]，给犬饲喂乳酸杆菌可以显著降低大肠杆菌的数量，增加有益菌双歧杆菌、乳酸杆菌的数目，同时增加粪便中乳酸和丁酸，并减少粪便氨、异丁酸、异戊酸和总支链脂肪酸的含量[34]，进而乳酸杆菌起到了保护肠道、抵御致病菌的作用。

(4) 改善肠道屏障。益生菌可通过降低旁分泌的通透性、增强黏膜层的抵抗力以及肠道物理屏障功能，从而预防和治疗细菌性腹泻等疾病[75]。肠黏膜由单层肠道上皮细胞及固有层组成，上皮层在最大限度吸收营养的同时，可以防止细菌和食物等成分的进入。上皮细胞中的杯状细胞分泌黏蛋白在上皮外形成黏液层(mucus)，抵御致病菌的入侵，干酪乳杆菌 DN-114001 可增加杯状细胞数目，从而使黏液层变厚以防止致病菌进入[76]。超过 80%的肠道上皮细胞为柱状细胞，邻近的细胞间形成紧密连接，以维持肠道正常的紧密性(细胞旁通透性和跨膜电阻是其测量指标)。致病菌可以通过上皮细胞发生易位或破坏紧密连接而突破肠道屏障。某些益生菌则可以通过改善肠道屏障来抵御致病菌，比如在 Caco-2 细胞系模型中，干酪乳杆菌逆转细胞因子诱导的跨膜电阻变小和上皮通透性增加，并调节 ZO-1 表达[77]，从而加强肠道机械屏障。

2.4 宠物用益生菌制剂存在的问题

如今，益生菌制剂在国内宠物市场兴起，用来调节宠物胃肠道健康，促进食物消化吸收，预防及控制宠物呕吐和腹泻等。益生菌虽已广泛应用于宠物，其实存在许多问题。有研究评估了 25 种商业动物用益生菌制剂，发现部分产品存在微生物标识不规范、说明书出现错误的问题，并且仅有 27%的产品的活菌数量达到标准[78]。另外，有研究评价了 19 种宠物用益生菌产品，同样发现产品与实际标签不符、活菌数目偏低，甚至存在其他微生物污染的问题[79]，这意味着目前宠物用益生菌制剂的质量参差不齐，把控十分不严格。

相比宠物益生菌制剂的质量问题，其安全性问题更值得人们关注，但目前相关研究报道甚少。益生菌毒性和可转移耐药基因的评定，是决定益生菌能否应用于市场的最关键因素。近年来，有研究发现常作为益生菌的蜡样芽孢杆菌可以高表达多种细菌毒素，并呈现多重耐药表型[80–82]。从国内商用益生菌制剂中分离的 65 种芽孢杆菌菌株，发现近一半能够产生有害毒素，典型菌株的

感染可引起败血症、肠道炎症和肝损伤[83]，其产生的肠毒素(non-hemolytic enterotoxin，Nhe)还可引起细胞凋亡[84]，原本用来治疗胃肠道疾病的蜡样芽孢杆菌，反而会导致呕吐和腹泻为特征的食物中毒暴发[85]。目前，还有研究发现动物用益生菌制剂中的致病菌可能会传染给人类，构成了对公共卫生安全的新威胁[86]。

因此，益生菌安全性要求和评估十分重要(图 3)。然而目前，还未有研究对国内的宠物用益生菌制剂进行系统的安全性评价，这意味着益生菌制剂可能已对宠物造成危害却不为人知。

3 展望

在我国，益生菌已广泛用于预防和治疗宠物细菌性腹泻，其具有抗菌效果好、提高宿主免疫力等优点，在未来的研发中越发受到重视。尽管如此，目前益生菌的筛选和应用仍存在许多问题，如相关法律法规不全面，对制剂的作用机理的研究不够深入，产品质量标准难以统一，以及存在安全隐患等。在未来，我国需尽快制定相应的小动物益生菌的使用标准，并继续探索未知的微生物群，开发潜在的动物源益生菌株，并做好安全性评价工作。

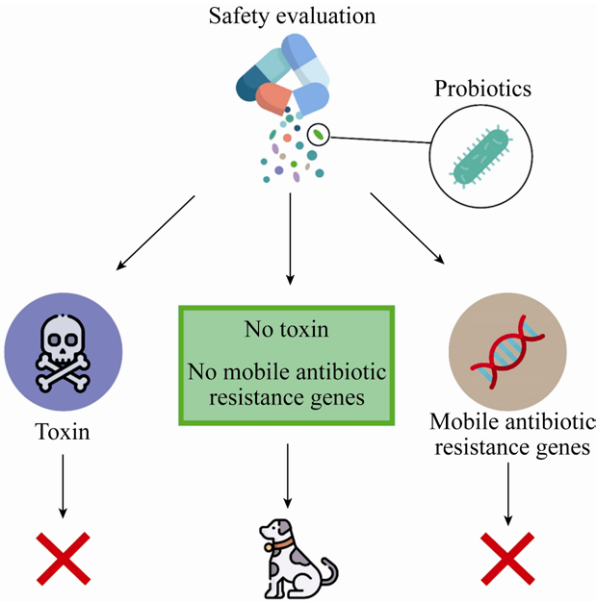

图 3. 中国宠物用益生菌的安全性评价

Figure 3. Safety evaluation of probiotics for companion animal use in China.

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Probiotics for treatment of bacterial diarrhea in pet animals

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Abstract: Antibacterial drugs have played important roles in treating bacterial diarrhea in pet animals; however, with the increase of bacterial resistance, the therapeutic effect of antibacterial drugs has been severely reduced. Probiotics are defined as “live microorganisms conferring health benefit on the host”, and have the potential for preventing, treating and healing bacterial diarrhea in pet animals. The application of probiotics in treating bacterial diarrhea is grossly promising. The species of bacterial pathogens, characteristics and prevention and treatment of current situation of diarrhea in pet animals, as well as the species, screening requirements, mechanisms, existing problems and application prospect of probiotics ameliorating gastrointestinal diseases in pet animals are reviewed.

Keywords: pet animals, bacterial diarrhea, probiotics

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