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甘露寡糖调控幼龄畜禽肠道健康机制的研究进展

晁洪雨[1]　杨　燕[2]　金太花[1]　吕慎金[1*]

(1.临沂大学农林科学学院,临沂 276003;2.临沂市农业科学院畜牧研究所,临沂 276003)

摘　要: 甘露寡糖(MOS)是一种主要由α-1,6和α-1,2糖苷键连接构成的甘露糖低聚体,通过改善幼龄畜禽肠道微生态平衡、加强肠黏膜屏障和免疫反应、调节肠道炎症、刺激小肠上皮细胞发育和减轻霉菌毒素及球虫病危害等调控措施,促进肠道健康和生产性能的提高,是未来畜禽养殖的抗生素促生长剂的理想替代品。本文总结了MOS调控幼龄畜禽肠道健康机制研究的最新进展,并探讨了未来的研究方向,旨在为进一步的研究和应用MOS提供理论依据。

关键词: 甘露寡糖;幼龄畜禽;微生态平衡;免疫增强;肠道健康

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现代集约化的生产易使幼龄畜禽面临各种不同的应激和病原体感染,引起机体病变和生长性能的下降,而加强肠道系统的营养供给是目前最常用的增强机体健康的方法[1]。肠道是微生物菌群、饲料抗原和免疫系统相互作用的主要场所[2],是机体抵御外界病原微生物及其有害代谢产物的先天性屏障,其健康与否是影响畜禽机体健康、内环境稳态和生产性能的重要因素[2-3]。肠道微生物菌群、形态学构造和肠黏膜免疫反应的平衡是维持肠道健康的主要特征[4]。肠道微生物菌群对营养物质代谢、病原微生物抵抗和免疫细胞发育起着非常重要的作用[5]。因此,畜禽肠道健康的维持主要依赖于饲粮的营养平衡和适宜的肠道微生态环境。

益生菌的添加能够改善后肠微生态平衡,保持肠道的良好健康状况。然而,益生菌活性在加工贮存过程及胃酸环境下容易受到破坏而影响饲用效果。相对而言,益生元较益生菌更具优势[6]。益生元是能够通过肠道微生物代谢而调节肠道微生物组成和(或)活性从而对宿主生理产生有益影响的不可被消化的食物成分[7],能够对肠道微生态结构与功能产生诸多影响,有利于畜禽健康和福利的改善。

来源于酵母细胞壁外层的甘露寡糖(MOS)由甘露糖、蛋白质、葡聚糖和磷酸根离子等构成[8],是主要由α-1,6和α-1,2糖苷键连接构成主链的甘露糖低聚体[9],是典型的功能性寡糖[10]和免疫性寡糖[11],也是一种能够促进畜禽健康和生长的益生元[12]。饲粮添加MOS能够改善肠道微生态平衡[13],提高宿主黏膜免疫力[14-16],减少腐败物质和氨的生成[17-18],益于肠道健康和生产性能的提高[19-22],是未来畜禽生产的抗生素促生长剂的理想替代品[23]。然而,MOS在畜禽饲喂中的实际应用效果并不完全一致,其原因可能与分子结构、添加水平、饲养环境、饲粮营养水平、畜禽年龄和健康状况等因素有关。因此,MOS的调控作用机制尚需更深入的研究和分析。通过查阅相关文献,本文综述了MOS调控幼龄畜禽肠道健康的机制研究进展,旨在为进一步的研究和应用MOS提供理论依据。

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作者简介:晁洪雨(1970—),男,山东临沂人,副教授,硕士,从事动物营养与饲料资源开发利用研究。E-mail: hongyuchao@126.com

* **通信作者:**吕慎金,教授,硕士生导师,E-mail: lvshenjin@lyu.edu.cn

1 加强肠黏膜屏障

肠道菌群和肠黏膜共同构成一道保护屏障,抵御外界病原微生物入侵。MOS 不能被胃和小肠消化吸收,因此能够提供大肠乳酸杆菌和双歧杆菌等有益菌的发酵底物[24],提高与致病菌争夺有限营养物质的竞争优势和占位,降低沙门氏菌等病原菌的吸附定植而选择性增殖有益菌群[25-27]。有益菌可与肠黏膜紧密结合构成肠道微生物屏障,抑制致病菌或条件性致病菌的过度生长,改善肠道的微生态平衡,对肠黏膜有保护和修复作用[28]。黏液素能够修复肠黏膜损伤[29],紧密连接蛋白能够维持旁细胞渗透和肠黏膜屏障功能[30]。有益菌群还可防止体内病原体引起的肠道上皮细胞结构和紧密连接蛋白的破裂,促进上皮细胞的增殖分化、黏液素的合成分泌[31-32]和富有黏液素的黏液数量的增加,提高肠道黏膜屏障的完整性[33],并在黏膜和微生物间形成黏液保护层,减少透过肠道屏障的细菌易位发生[34],保护肠道微生物屏障。

MOS 也能够直接促进肠黏膜黏液素的分泌[35],提高黏液素和热应激条件下紧密连接蛋白及封闭蛋白的 mRNA 表达丰度[22,35],并维持肠黏膜屏障细胞结构和紧密连接结构[36],有效缓解肠炎沙门氏菌引起的 Caco-2 细胞膜屏障功能的损伤[37],从而改善畜禽肠黏膜屏障功能。

超氧化物歧化酶(SOD)是清除机体游离基的十分重要的一种抗氧化酶,丙二醛(MDA)是脂质过氧化作用的最终产物,是衡量脂质过氧化作用的重要指标。MOS 能够提高机体 SOD 等抗氧化酶活性,清除游离基,抑制机体组织和(或)禽蛋脂质的过氧化作用[15-16,38],显著降低热应激状态下肉仔鸡空肠黏膜的 MDA 含量,缓解热应激引起的肠黏膜氧化损伤,提高肠黏膜抗氧化能力和肠道健康[22]。

2 抑制肠道病原菌的黏附定植

黏附定植能力是病原菌重要的毒性特征之一。病原菌与肠道细胞的黏附作用是其定植并产生临床症状的重要前提条件,是产生致病作用的重要步骤。病原菌细胞表面含有能够键合碳水化合物的蛋白质——外源凝集素,病原菌可通过外源凝集素与肠黏膜低聚糖结构变体结合而黏附定植,引起病变。MOS 中的甘露糖残基能够与表达Ⅰ型菌毛的埃希氏大肠杆菌[39]和沙门氏菌[40]等革兰氏阴性病原菌的甘露糖特定凝集素结合,从而阻止或减少病原菌在肠黏膜上的定植黏附,促进病原菌的肠道排泄[41]。除了能与肠道有害菌结合以外,MOS 中的有效成分之一——α-*D*-甘露糖,还可作为一种配体与肠黏膜上皮细胞表面相应的受体——α-*D*-甘露糖受体特异性识别,当其达到一定浓度时,已经定植在肠黏膜上皮的病原菌就被竞争性脱离下来而排出体外[42],从而打断了病原菌附着-繁殖-致病的途径,改善了动物的肠道健康状况。当然,由于化学组成结构(甘露糖构成比例和糖苷键)的不同,MOS 对肠道埃希氏大肠杆菌和沙门氏菌数量的调控效率可能存在较大差异[43]。

3 促进肠道有益菌产生抑制病原微生物的代谢产物

肠道微生物菌群处于一个动态变化过程中,某种微生物数量的增加可能引起另一种微生物数量的降低。饲粮添加 MOS 导致的肠道病原微生物数量的减少与有益菌群特别是乳酸杆菌数量的增加密切相关[44-45]。这些有益菌群能够代谢产生细菌素、促肠活动素、过氧化氢和相关诱导酶,促进有益菌群的竞争和发育[46]。细菌素是一类选择性作用于细菌靶细胞的抗菌物质,通过激活巨噬细胞、刺激抗体生成和抗肿瘤因素对病原微生物产生抑制作用[47]。过氧化氢可激活肠道中的过氧化物酶-硫氰酸盐反应系统,使乳酸过氧化酶与过氧化氢结合,再将硫氰酸盐氧化成氧化性中间产物,抑制致病菌的生长和繁殖[48]。胞外糖苷酶等诱导酶可降解肠黏膜上皮细胞的复杂多糖,从而减少致病菌和细菌毒素的潜在受体,阻止致病菌对肠道上皮细胞的侵袭[49]。

4 提高肠内容物短链脂肪酸含量,调节肠道炎症

MOS 能够促进后肠乳酸杆菌、双歧杆菌和盲肠拟杆菌门细菌的增殖[50-51],有效发酵不消化的多糖,利于乳酸和(或)丁酸、丙酸及乙酸等短链脂肪酸的生成[52-54]。短链脂肪酸不仅提供肠道上皮细胞能量,促进上皮细胞正常增殖和分化[55],改善

肠道黏膜的完整性[6,56],而且能够抑制鼠伤寒沙门氏菌[57]和肠出血性大肠杆菌[58]等病原菌黏附因子或致病基因的表达,阻止病原微生物对肠组织的侵袭。同时,短链脂肪酸还可降低肠腔局部pH,抑制不耐酸腐败菌和致病菌的生长繁殖[59],并一定程度上利于乳酸杆菌的增殖[60],从而调节肠道炎症及其代谢功能[31]。此外,丁酸也可抑制肠系膜淋巴结干扰素-α(IFN-α)和白细胞介素-2(IL-2)[61]、Caco-2 细胞趋化因子-8(CXCL-8)[62]、单核细胞肿瘤坏死因子-α(TNF-α)[63]和盲肠扁桃体 Toll 样受体-2(TLR-2)、回肠白细胞介素-12 p35(IL-12 p35)及干扰素-γ(IFN-γ)[64]等促炎症细胞因子的产生,降低核转录因子-κB(NF-κB)活性,提高细胞质抑制剂水平,从而减少促炎症趋化因子和细胞因子的生成[61,65]。与果寡糖和半乳寡糖一样,MOS 调节肠道炎症的原因可能还与普拉梭菌(*Faecalibacterium prausnitzii*)等产丁酸菌的丰度增加有关。普拉梭菌等产丁酸菌能够抑制促炎症细胞因子的产生,诱导白细胞介素-10(IL-10)等抗炎症细胞因子的生成[66-67],从而抑制 T 细胞、自然杀伤(NK)细胞和巨噬细胞功能,避免肠道过度的炎症反应。

5　调控肠道免疫反应

MOS 通过增殖肠道有益菌、降低病原菌的着床、调节肠道微生物菌群的构成和功能,增强肠道的局部免疫应答和免疫指标[68],从而引发机体的系统免疫反应。MOS 增殖的有益菌通过肠道上皮细胞对机体的特异性免疫和非特异性免疫进行调节,增加肠道成熟 T 细胞数量和外周血液 $CD4^+$ T 淋巴细胞数量及 $CD4^+/CD8^+$[69],增强 T 淋巴细胞和 B 淋巴细胞的活性,提高机体的细胞免疫和体液免疫功能。肠道有益微生物菌群也可穿过肠道屏障进入派尔集合淋巴结,激活免疫细胞[70]。同时,MOS 发酵产生的短链脂肪酸既可引起 NK 细胞数量上升[71],活性增强,又可增加 $CD4^+$ 和 TCR-2淋巴细胞数量,从而通过抗原提呈细胞激活对外源抗原的免疫应答[72],对免疫系统产生显著的影响。例如结肠内环境的酸化既有益于肠道绒毛的杯状细胞分泌黏液素,抑制有害病原菌的肠道吸附,又容易使短链脂肪酸与肠道淋巴组织免疫细胞的短链脂肪酸受体结合[73],调节肠道的免疫能力。

畜禽肠黏膜上皮细胞和吞噬细胞能够分泌宿主防御肽[74-75]。宿主防御肽是一类具有抗菌、抗癌、抗病毒和修复损伤及免疫调节等作用的多功能肽,是机体抵抗病原入侵的第 1 道屏障[76],能够通过募集和激活不同类型的免疫细胞调节宿主免疫系统[77]。MOS 增殖的肠道乳酸杆菌和大肠发酵产生的丁酸等短链脂肪酸具有强烈的诱导宿主防御肽表达分泌的能力[78-81],能够有效诱导合成鸡 HD11 巨噬细胞和初级单核细胞中的宿主防御肽[80]。而且更重要的是,丁酸等短链脂肪酸增强了宿主防御肽基因的表达,但却不刺激促炎症细胞因子白细胞介素-1β(IL-1β)的产生[82]。

Toll 样受体(TLR)是参与非特异性免疫的一类重要蛋白质分子,也是连接非特异性免疫和特异性免疫的桥梁。TLR-4 和 TLR-2 能够识别 MOS[54],饲喂 MOS 能够增加回肠或盲肠扁桃体 *TLR*-4 和 *TLR*-2 的表达[83]。畜禽巨噬细胞和嗜异性白细胞 *TLR*-4 mRNA 表达量较高[84],当 TLR-4 识别脂多糖等病原相关分子模式后,免疫细胞能够产生较高水平的一氧化氮和促炎症细胞因子,抵抗病原菌的侵袭[54]。因此,MOS 能够通过降低埃希氏大肠杆菌脂多糖含量,减少 *TLR*-4 的基因表达,抑制促炎症免疫反应[83]。然而,MOS 分子自身也能够被 TLR-4 识别,作为促炎症因子增强 *TLR*-4 基因表达,诱发非特异性免疫应答[85]。同样,TLR-2 也可通过识别 MOS 分子引起促炎症细胞因子级联反应。此外,MOS 还能够增强回肠 *IL*-12和 *IFN*-γ 的基因表达[83]。IL-12可激活辅助 T 细胞 1,触发 IFN-γ 释放,引起 T 细胞、NK 细胞和巨噬细胞等免疫细胞的增殖和细胞毒性[86]。

MOS 不仅通过优先增殖的有益微生物及代谢产物与免疫细胞的间接作用调控肠道免疫反应,而且还能够直接作用于肠道免疫细胞[87],增加补体含量和溶菌酶活性[88],增强免疫力。MOS 能够刺激肠道甘露糖结合蛋白和抗甘露聚糖抗体的生成[89]。甘露糖结合蛋白可通过碳水化合物识别域特异性地识别多种病原微生物,并与其表面的甘露糖残基和(或)N-乙酰葡萄糖胺结合,引起甘露糖结合蛋白构象的改变,从而与吞噬细胞表面的胶原凝集素受体结合而激活吞噬细胞,增强吞噬细胞的吞噬作用和补体系统的激活[90]。吞噬细胞激活后,一方面直接通过吞噬作用将入侵的各类病原体包括自身代谢产生的有害有毒物质灭杀清

除;另一方面,在免疫应答的初期阶段,吞噬细胞可将抗原降解并将抗原信号呈递给其他淋巴细胞,启动后天性免疫应答反应[91]。抗甘露聚糖抗体是甘露聚糖的天然抗体,是与肠道微生物作用的正常免疫应答,可直接特异性地结合病毒和细菌的寡糖类抗原决定簇,引起病毒和细菌的调理作用,增强吞噬细胞的吞噬作用[9,92]。除此之外,MOS 还可激活吞噬细胞胞内信号通路,产生 IL、IFN 及 TNF 等细胞因子,通过它们的协同作用增强机体的免疫机能[93-94]。关于 MOS 直接刺激肠道免疫细胞增强免疫力的详细作用机理目前尚不甚清晰,还需对无菌动物模型进行更多的研究加以证实。

6 改善肠道形态学构造,促进幼龄畜禽的肠道发育

MOS 在肠道发酵产生的丁酸能够促进肠道细胞发育和绒毛生长,增加幼龄畜禽肠道隐窝深度、绒毛高度、绒毛高度/隐窝深度和绒毛表面积[29,35,89,95-97],缓解埃希氏大肠杆菌攻毒和热应激对动物肠道的损伤[22,98-99]。隐窝深度的增加表明干细胞增殖数量增多,引起分泌黏液素的杯状细胞数量增加。绒毛高度和表面积的增加有利于提高肠道锌、铜、硒等微量元素的吸收,增强免疫力[100]。总体而言,肠道菌群对 MOS 的发酵能够提供肠道上皮细胞营养物质,促进细胞的增殖分化和更新[101],利于黏液层生成[68]和肠道黏膜细胞的恢复[102],加快畜禽早期肠道的发育和成熟[103-104],提高肠道的吸收效率[16,105],减少幼龄畜禽肠道疾病的发生。

7 提升饲料品质,减轻霉菌毒素和球虫病危害

霉菌毒素是毒性很强的霉菌次生代谢产物,是一种广泛存在于饲料和原料中的抗营养因子。由于真菌代谢产物的独特性质,生产中很难将霉菌毒素从饲料和原料中清除干净[106]。霉菌毒素易降低畜禽食欲[107]和饲料营养物质的消化吸收[108],降低肠道免疫球蛋白的分泌水平和养分运载体基因的相对表达量[109],加快肠道病原菌增殖[110],损害小肠绒毛形态结构[110-111],不利于畜禽肠道健康和生长发育[110]。MOS 既能够通过物理吸附或直接结合等方式与饲料中的霉菌毒素结合,改善饲料品质,也可螯合胃肠道释放的黄曲霉毒素,减轻肠道对霉菌毒素的吸收和霉菌毒素对肠道的危害[112-113],从而降低肝脏霉菌毒素含量,减轻肝脏损伤[114],增强畜禽肠道健康,改善营养物质消化吸收,提高饲料利用效率,促进生产性能的提高[110,115]。

球虫常寄生于畜禽肠黏膜上皮细胞内,致病性强,危害性大。MOS 不仅能够减少粪便中的球虫卵囊数量,提高球虫感染后肠道促炎性因子的分泌水平[116],也可提高机体在球虫感染后 *IFN-γ* mRNA 的表达量[117],减轻肠黏膜损伤。

8 小 结

近年来,为改善畜禽健康和福利,应对饲料行业“限抗、禁抗和替抗”问题,营养学家利用糖生物学和糖生物技术,对 MOS 在畜禽肠道内的代谢和参与机体炎症、病原体感染及肠道免疫和发育的机理进行了深入研究和分析,为 MOS 在畜禽养殖中的应用奠定了良好的基础。但幼龄畜禽肠道发育不完善,易受外界不良因素的影响产生应激,MOS 的调控机制与途径目前尚未完全清晰,还存在诸多未能解决的问题,从而制约了养殖业中的推广应用。因此,今后需要进一步加强对 MOS 理化结构与其功能的内在关系以及不同动物、不同生理状态下肠道内作用机理的研究和探讨,明确和指导 MOS 的最佳利用方式,以广泛有效地应用于畜禽生产实践中。

参考文献:

[1] PERRY B D, GRACE D, SONES K. Current drivers and future directions of global livestock disease dynamics[J]. Proceedings of the National Academy of Sciences of the United States of America, 2013, 110(52): 20871-20877.

[2] BRISBIN J T, GONG J, SHARIF S. Interactions between commensal bacteria and the gut-associated immune system of the chicken[J]. Animal Health Research Reviews, 2008, 9(1): 101-110.

[3] YEGANI M, KORVER D R. Factors affecting intestinal health in poultry[J]. Poultry Science, 2008, 87(10): 2052-2063.

[4] CHOCT M. Managing gut health through nutrition[J]. British Poultry Science, 2009, 50(1): 9-15.

[5] LEE W J, HASE K. Gut microbiota-generated metabolites in animal health and disease[J]. Nature Chemical Biology, 2014, 10(6): 416-424.

[6] ALLOUI M N, SZCZUREK W, ŚWIATKIEWICZ S. The usefulness of prebiotics and probiotics in modern poultry nutrition: a review[J]. Annals of Animal Science, 2013, 13(1): 17-32.

[7] BINDELS L B, DELZENNE N M, CANI P D, et al. Towards a more comprehensive concept for prebiotics [J]. Nature Reviews Gastroenterology & Hepatology, 2015, 12(5): 303-310.

[8] KLIS F M, MOL P, HELLINGWERF K, et al. Dynamics of cell wall structure in *Saccharomyces cerevisiae*[J]. FEMS Microbiology Reviews, 2002, 26(3): 239-256.

[9] HALAS V, NOCHTA I. Mannan oligosaccharides in nursery pig nutrition and their potential mode of action [J]. Animals, 2012, 2(2): 261-274.

[10] PATEL S, GOYAL A. Functional oligosaccharides: production, properties and applications [J]. World Journal of Microbiology and Biotechnology, 2011, 27 (5): 1119-1128.

[11] SONG S K, BECK B R, KIM D, et al. Prebiotics as immunostimulants in aquaculture: a review[J]. Fish & Shellfish Immunology, 2014, 40(1): 40-48.

[12] CHE T M, JOHNSON R W, KELLEY K W, et al. Mannan oligosaccharide improves immune responses and growth efficiency of nursery pigs experimentally infected with porcine reproductive and respiratory syndrome virus[J]. Journal of Animal Science, 2011, 89 (8): 2592-2602.

[13] CASTILLO M, MARTÍN-ORÚE S M, TAYLOR-PICKARD J A, et al. Use of mannanoligosaccharides and zinc chelate as growth promoters and diarrhea preventative in weaning pigs: effects on microbiota and gut function[J]. Journal of Animal Science, 2008, 86 (1): 94-101.

[14] CHENG G Y, HAO H H, XIE S Y, et al. Antibiotic alternatives: the substitution of antibiotics in animal husbandry[J]. Frontiers in Microbiology, 2014, 5: 217.

[15] ATTIA Y A, AL-KHALAIFAH H, IBRAHIM M S, et al. Blood hematological and biochemical constituents, antioxidant enzymes, immunity and lymphoid organs of broiler chicks supplemented with propolis, bee pollen and mannan oligosaccharides continuously or intermittently[J]. Poultry Science, 2017, 96(12): 4182-4192.

[16] ZHENG C, LI F D, HAO Z L, et al. Effects of adding mannan oligosaccharides on digestibility and metabolism of nutrients, ruminal fermentation parameters, immunity, and antioxidant capacity of sheep[J]. Journal of Animal Science, 2018, 96(1): 284-292.

[17] JUŚKIEWICZ J, ZDUŃCZYK Z, JANKOWSKI J. Effect of adding mannan-oligosaccharide to the diet on the performance, weight of digestive tract segments, and caecal digesta parameters in young turkeys[J]. Journal of Animal and Feed Sciences, 2003, 12(1): 133-142.

[18] DOS SANTOS FELSSNER K, TODESCO H, GRANDE P A, et al. Dietetic combination of mannan-oligosaccharides and fructooligosaccharides modifies nitrogen metabolism in dogs [J]. Semina: Ciências Agrárias, 2016, 37(5): 3335-3348.

[19] ZHAO P Y, JUNG J H, KIM I H. Effect of mannan oligosaccharides and fructan on growth performance, nutrient digestibility, blood profile, and diarrhea score in weanling pigs[J]. Journal of Animal Science, 2012, 90 (3): 833-839.

[20] ATTIA Y A, AL-HAMID A E A, IBRAHIM M S, et al. Productive performance, biochemical and hematological traits of broiler chickens supplemented with propolis, bee pollen, and mannan oligosaccharides continuously or intermittently [J]. Livestock Science, 2014, 164: 87-95.

[21] CHENG Y F, DU M F, XU Q, et al. Dietary mannan oligosaccharide improves growth performance, muscle oxidative status, and meat quality in broilers under cyclic heat stress[J]. Journal of Thermal Biology, 2018, 75: 106-111.

[22] CHENG Y F, CHEN Y P, CHEN R, et al. Dietary mannan oligosaccharide ameliorates cyclic heat stress-induced damages on intestinal oxidative status and barrier integrity of broilers[J]. Poultry Science, 2019: pez192, doi: 10.3382/ps/pez192.

[23] SAEED M, AHMAD F, ASIF ARAIN M, et al. Use of mannan-oligosaccharides (MOS) as a feed additive in poultry nutrition[J]. Journal of World's Poultry Research, 2017, 7(3): 94-103.

[24] HAJATI H, REZAEI M. The application of prebiotics in poultry production[J]. International Journal of Poultry Science, 2010, 9(3): 298-304.

[25] KIM G B, SEO Y M, KIM C H, et al. Effect of dietary prebiotic supplementation on the performance, intestinal microflora, and immune response of broilers[J]. Poultry Science, 2011, 90(1): 75-82.

[26] SPRING P, WENK C, CONNOLLY A, et al. A review of 733 published trials on Bio-Mos ®, a mannan oligosaccharide, and Actigen ®, a second generation mannose rich fraction, on farm and companion animals [J]. Journal of Applied Animal Nutrition, 2015, 3: e8.

[27] ADHIKARI P A, KIM W K. Overview of prebiotics and probiotics: focus on performance, gut health and immunity—a review [J]. Annals of Animal Science, 2017, 17(4): 949-966.

[28] KICZOROWSKA B, SAMOLIŃSKA W, AL-YASIRY A R M, et al. The natural feed additives as immunostimulants in monogastric animal nutrition—a review [J]. Annals of Animal Science, 2017, 17(3): 605-625.

[29] HUTSKO S L, MEIZLISCH K, WICK M, et al. Early intestinal development and mucin transcription in the young poult with probiotic and mannan oligosaccharide prebiotic supplementation [J]. Poultry Science, 2016, 95(5): 1173-1178.

[30] ULLUWISHEWA D, ANDERSON R C, MCNABB W C, et al. Regulation of tight junction permeability by intestinal bacteria and dietary components [J]. The Journal of Nutrition, 2011, 141(5): 769-776.

[31] POURABEDIN M, XU Z X, BAURHOO B, et al. Effects of mannan oligosaccharide and virginiamycin on the cecal microbial community and intestinal morphology of chickens raised under suboptimal conditions [J]. Canadian Journal of Microbiology, 2014, 60(5): 255-266.

[32] RAJANI J, DASTAR B, SAMADI F, et al. Effect of extracted galactoglucomannan oligosaccharides from pine wood (*Pinus brutia*) on *Salmonella typhimurium* colonisation, growth performance and intestinal morphology in broiler chicks [J]. British Poultry Science, 2016, 57(5): 682-692.

[33] IJI P A, TIVEY D R. Natural and synthetic oligosaccharides in broiler chicken diets [J]. World's Poultry Science Journal, 1998, 54(2): 129-143.

[34] SCHLEY P D, FIELD C J. The immune-enhancing effects of dietary fibres and prebiotics [J]. British Journal of Nutrition, 2002, 87(S2): S221-S230.

[35] CHELED-SHOVAL S L, AMIT-ROMACH E, BARBAKOV M, et al. The effect of in ovo administration of mannan oligosaccharide on small intestine development during the pre- and posthatch periods in chickens [J]. Poultry Science, 2011, 90(10): 2301-2310.

[36] TORRECILLAS S, MAKOL A, BETANCOR M B, et al. Enhanced intestinal epithelial barrier health status on European sea bass (*Dicentrarchus labrax*) fed mannan oligosaccharides [J]. Fish & Shellfish Immunology, 2013, 34(6): 1485-1495.

[37] BRUFAU M T, CAMPO-SABARIZ J, BOU R, et al. Salmosan, a β-galactomannan-rich product, protects epithelial barrier function in Caco-2 cells infected by *Salmonella enterica* serovar enteritidis [J]. The Journal of Nutrition, 2016, 146(8): 1492-1498.

[38] BOZKURT M, TOKUŞOĞLU Ö, KÜÇÜKYILMAZ K, et al. Effects of dietary mannan oligosaccharide and herbal essential oil blend supplementation on performance and oxidative stability of eggs and liver in laying hens [J]. Italian Journal of Animal Science, 2012, 11(2): e41.

[39] FESSELE C, LINDHORST T K. Effect of aminophenyl and aminothiahexyl α-*D*-glycosides of the manno-, gluco-, and galacto-series on type 1 fimbriae-mediated adhesion of *Escherichia coli* [J]. Biology, 2013, 2(3): 1135-1149.

[40] ADEWOLE D I, KIM I H, NYACHOTI C M. Gut health of pigs: challenge models and response criteria with a critical analysis of the effectiveness of selected feed additives—a review [J]. Asian-Australasian Journal of Animal Sciences, 2016, 29(7): 909-924.

[41] THOMAS W E, NILSSON L M, FORERO M, et al. Shear-dependent 'stick-and-roll' adhesion of type 1 fimbriated *Escherichia coli* [J]. Molecular Microbiology, 2004, 53(5): 1545-1557.

[42] FIRON N, OFEK I, SHARON N. Interaction of mannose-containing oligosaccharides with the fimbrial lectin of *Escherichia coli* [J]. Biochemical and Biophysical Research Communications, 1982, 105(4): 1426-1432.

[43] SINGBROOTA P. Agglutination of type-1 fimbrial bacteria by different yeast cell wall products [D]. Ph.D. Thesis. Raleigh, NC, USA: North Carolina State University, 2005: 41-63.

[44] JAHANIAN R, ASHNAGAR M. Effect of dietary supplementation of mannan-oligosaccharides on performance, blood metabolites, ileal nutrient digestibility, and gut microflora in *Escherichia coli*-challenged laying hens [J]. Poultry Science, 2015, 94(9): 2165-2172.

[45] REKIEL A, WIECEK J, BIELECKI W, et al. Effect of addition of feed antibiotic flavomycin or prebiotic BIO-MOS on production results of fatteners, blood biochemical parameters, morphometric indices of intes-

tine and composition of microflora[J]. Archives of Tierz Dummerstorf,2007,50:172-180.

[46] LEROY F,FOULQUIÉ MORENO M R,DE VUYST L.*Enterococcus faecium* RZS C5,an interesting bacteriocin producer to be used as a co-culture in food fermentation[J].International Journal of Food Microbiology,2003,88(2/3):235-240.

[47] VAMANU E,VAMANU A.The influence of prebiotics on bacteriocin synthesis using the strain *Lactobacillus paracasei* CMGB16[J].African Journal of Microbiology Research,2010,4(7):534-537.

[48] YU J,WANG W H,MENGHE B L G,et al.Diversity of lactic acid bacteria associated with traditional fermented dairy products in Mongolia[J]. Journal of Dairy Science,2011,94(7):3229-3241.

[49] 谢强,李孟孟,王文策,等.益生菌对家禽肠道微生态的调控及其应用[J].饲料研究,2017(2):30-36.

[50] CORRIGAN A,DE LEEUW M,PENAUD-FRÉZET S,et al.Phylogenetic and functional alterations in bacterial community compositions in broiler ceca as a result of mannan oligosaccharide supplementation[J]. Applied and Environmental Microbiology, 2015, 81(10):3460-3470.

[51] LEE S I,PARK S H,RICKE S C.Assessment of cecal microbiota,integron occurrence,fermentation responses,and *Salmonella* frequency in conventionally raised broilers fed a commercial yeast-based prebiotic compound[J].Poultry Science,2016,95(1):144-153.

[52] POEIKHAMPHA T,BUNCHASAK C. Comparative effects of sodium gluconate,mannan oligosaccharide and potassium diformate on growth performances and small intestinal morphology of nursery pigs[J].Asian-Australasian Journal of Animal Sciences, 2011, 24(6):844-850.

[53] BOVERA F,LESTINGI A,MARONO S,et al.Effect of dietary mannan-oligosaccharides on *in vivo* performance,nutrient digestibility and caecal content characteristics of growing rabbits[J].Journal of Animal Physiology and Animal Nutrition,2012,96(1):130-136.

[54] TENG P Y,KIM W K.Review:roles of prebiotics in intestinal ecosystem of broilers[J].Frontiers in Veterinary Science,2018,5:245.

[55] FOUHSE J M,ZIJLSTRA R T,WILLING B P.The role of gut microbiota in the health and disease of pigs[J].Animal Frontiers,2016,6(3):30-36.

[56] EMAMI N K,NAEINI S Z,RUIZ-FERIA C A. Growth performance,digestibility,immune response and intestinal morphology of male broilers fed phosphorus deficient diets supplemented with microbial phytase and organic acids[J]. Livestock Science,2013,157(2/3):506-513.

[57] SUN Y,O'RIORDAN M X D.Regulation of bacterial pathogenesis by intestinal short-chain fatty acids[J]. Advances in Applied Microbiology,2013,85:93-118.

[58] SPRING P,WENK C,DAWSON K A,et al. The effects of dietary mannaoligosaccharides on cecal parameters and the concentrations of enteric bacteria in the ceca of *Salmonella*-challenged broiler chicks[J]. Poultry Science,2000,79(2):205-211.

[59] KAUR P,CHAKRABORTI A.Proteome analysis of a food borne pathogen enteroaggregative *Escherichia coli* under acid stress[J]. Journal of Proteomics & Bioinformatics,2010,3(1):10-19.

[60] HOPKINS M J,MACFARLANE G T.Nondigestible oligosaccharides enhance bacterial colonization resistance against *Clostridium difficile in vitro*[J].Applied and Environmental Microbiology,2003,69(4):1920-1927.

[61] TEDELIND S,WESTBERG F,KJERRULF M,et al. Anti-inflammatory properties of the short-chain fatty acids acetate and propionate:a study with relevance to inflammatory bowel disease[J]. World Journal of Gastroenterology,2007,13(20):2826-2832.

[62] WENG M Q,WALKER W A,SANDERSON I R.Butyrate regulates the expression of pathogen-triggered *IL*-8 in intestinal epithelia[J]. Pediatric Research,2007,62(5):542-546.

[63] RODRÍGUEZ-CABEZAS M E,GÁLVEZ J,CAMUESCO D,et al.Intestinal anti-inflammatory activity of dietary fiber (*Plantago ovata* seeds) in HLA-B27 transgenic rats[J]. Clinical Nutrition, 2003, 22(5):463-471.

[64] RODRÍGUEZ-LECOMPTE J C,YITBAREK A,BRADY J,et al.The effect of microbial-nutrient interaction on the immune system of young chicks after early probiotic and organic acid administration[J]. Journal of Animal Science,2012,90(7):2246-2254.

[65] SEGAIN J P,RAINGEARD DE LA BLÉTIÈRE D,BOURREILLE A,et al.Butyrate inhibits inflammatory responses through NFκB inhibition:implications for Crohn's disease[J].Gut,2000,47(3):397-403.

[66] HART A L,LAMMERS K,BRIGIDI P,et al.Modulation of human dendritic cell phenotype and function by

probiotic bacteria[J].Gut,2004,53(11):1602-1609.

[67] ROSSI O,VAN BERKEL L A,CHAIN F,et al.*Faecalibacterium prausnitzii* A2-165 has a high capacity to induce IL-10 in human and murine dendritic cells and modulates T cell responses[J].Scientific Reports,2016,6:18507.

[68] ROBERFROID M,GIBSON G R,HOYLES L,et al.Prebiotic effects:metabolic and health benefits[J].British Journal of Nutrition,2010,104:S1-S63.

[69] MAHESH M,PAWAR,ASHOK K,et al.Effect of dietary mannanoligosaccharide supplementation on nutrient digestibility,hindgut fermentation,immune response and antioxidant indices in dogs[J].Journal of Animal Science and Technology,2017,59:11.

[70] BERG R D.Indigenous intestinal microflora and the host immune response[J].EOS Journal of Immunology and Immunopharmacology,1985,4:161-168.

[71] KELLY-QUAGLIANA K A,BUDDINGTON R,VAN LOO J,et al.Immunomodulation by oligofructose and inulin[J].FASEB Journal,1998,12(5):904.

[72] KHAN S H,IQBAL J.Recent advances in the role of organic acids in poultry nutrition[J].Journal of Applied Animal Research,2016,44(1):359-369.

[73] LOMAX A R,CALDER P C.Prebiotics,immune function,infection and inflammation:a review of the evidence[J].British Journal of Nutrition,2009,101(5):633-658.

[74] PASUPULETI M,SCHMIDTCHEN A,MALMSTEN M.Antimicrobial peptides:key components of the innate immune system[J].Critical Reviews in Biotechnology,2012,32(2):143-171.

[75] TAKAHASHI D,SHUKLA S K,PRAKASH O,et al.Structural determinants of host defense peptides for antimicrobial activity and target cell selectivity[J].Biochimie,2010,92(9):1236-1241.

[76] 窦秀静,韩俊兰,徐欣瑶,等.动物内源性宿主防御肽的表达调控[C]//中国畜牧兽医学会动物营养学分会第十二次动物营养学术研讨会论文集.武汉:中国畜牧兽医学会,2016:641.

[77] CHOI K Y G,CHOW L N Y,MOOKHERJEE N.Cationic host defence peptides:multifaceted role in immune modulation and inflammation[J].Journal of Innate Immunity,2012,4(4):361-370.

[78] ZHANG J H,DENG J,LI Y F,et al.The effect of *Lactobacillus* on the expression of porcine β-defensin-2 in the digestive tract of piglets[J].Livestock Science,2011,138(1/2/3):259-265.

[79] SUNKARA L T,ACHANTA M,SCHREIBER N B,et al.Butyrate enhances disease resistance of chickens by inducing antimicrobial host defense peptide gene expression[J].PLoS One,2011,6(11):e27225.

[80] SUNKARA L T,JIANG W,ZHANG G L.Modulation of antimicrobial host defense peptide gene expression by free fatty acids[J].PLoS One,2012,7(11):e49558.

[81] ZENG X F,SUNKARA L T,JIANG W Y,et al.Induction of porcine host defense peptide gene expression by short-chain fatty acids and their analogs[J].PLoS One,2013,8(8):e72922.

[82] 王鑫,张萌萌,姜宁,等.宿主防御肽调节动物肠道屏障功能的研究进展[J].动物营养学报,2018,30(9):3410-3416.

[83] YITBAREK A,ECHEVERRY H,BRADY J,et al.Innate immune response to yeast-derived carbohydrates in broiler chickens fed organic diets and challenged with *Clostridium perfringens*[J].Poultry Science,2012,91(5):1105-1112.

[84] JUUL-MADSEN H R,VIERTLBÖECK B,HÄRTLE S,et al.Innate immune responses[M]//SCHAT K A,KASPERS B,KAISER P.Avian immunology.2nd ed.Boston,MA:Academic Press,2014:121-147.

[85] TADA H,NEMOTO E,SHIMAUCHI H,et al.*Saccharomyces cerevisiae*- and *Candida albicans*-derived mannan induced production of tumor necrosis factor alpha by human monocytes in a CD14- and toll-like receptor 4-dependent manner[J].Microbiology and Immunology,2002,46(7):503-512.

[86] TIZARD I R.Veterinary immunology[M].9th ed.Amsterdam:Elsevier,2013.

[87] JANARDHANA V,BROADWAY M M,BRUCE M P,et al.Prebiotics modulate immune responses in the gut-associated lymphoid tissue of chickens[J].The Journal of Nutrition,2009,139(7):1404-1409.

[88] DUAN X D,CHEN D W,ZHENG P,et al.Effects of dietary mannan oligosaccharide supplementation on performance and immune response of sows and their offspring[J].Animal Feed Science and Technology,2016,218:17-25.

[89] SHEN Y B,PIAO X S,KIM S W,et al.Effects of yeast culture supplementation on growth performance,intestinal health,and immune response of nursery pigs[J].Journal of Animal Science,2009,87(8):2614-2624.

[90] DOMMETT R M, KLEIN N, TURNER M W. Mannose-binding lectin in innate immunity: past, present and future[J]. Tissue Antigens, 2006, 68(3): 193-209.

[91] 陈梁城. 酵母多糖(β-葡聚糖和甘露寡糖)对动物抗病的调控作用研究[D]. 博士学位论文. 长春: 吉林农业大学, 2015: 13.

[92] NOCHTA I, TUBOLY T, HALAS V, et al. Effect of different levels of mannan-oligosaccharide supplementation on some immunological variables in weaned piglets[J]. Journal of Animal Physiology and Animal Nutrition, 2009, 93(4): 496-504.

[93] SHENG K C, POUNIOTIS D S, WRIGHT M D, et al. Mannan derivatives induce phenotypic and functional maturation of mouse dendritic cells[J]. Immunology, 2006, 118(3): 372-383.

[94] RAETZ C R H, WHITFIELD C. Lipopolysaccharide endotoxins[J]. Annual Review of Biochemistry, 2002, 71: 635-700.

[95] AHSAN U, CENGĪZ Ö, RAZA I, et al. Sodium butyrate in chicken nutrition: the dynamics of performance, gut microbiota, gut morphology, and immunity[J]. World's Poultry Science Journal, 2016, 72(2): 265-275.

[96] IJI P A, SAKI A A, IVEY D R. Intestinal structure and function of broiler chickens on diets supplemented with a mannan oligosaccharide[J]. Journal of the Science of Food and Agriculture, 2001, 81(12): 1186-1192.

[97] ZHAO J, HARPER A F, ESTIENNE M J, et al. Growth performance and intestinal morphology responses in early weaned pigs to supplementation of antibiotic-free diets with an organic copper complex and spray-dried plasma protein in sanitary and nonsanitary environments[J]. Journal of Animal Science, 2007, 85(5): 1302-1310.

[98] WANG W W, LI Z, HAN Q Q, et al. Dietary live yeast and mannan-oligosaccharide supplementation attenuate intestinal inflammation and barrier dysfunction induced by *Escherichia coli* in broilers[J]. British Journal of Nutrition, 2016, 116(11): 1878-1888.

[99] SOHAIL M U, HUME M E, BYRD J A, et al. Effect of supplementation of prebiotic mannan-oligosaccharides and probiotic mixture on growth performance of broilers subjected to chronic heat stress[J]. Poultry Science, 2012, 91(9): 2235-2240.

[100] SHASHIDHARA R G, DEVEGOWDA G. Effect of dietary mannan oligosaccharide on broiler breeder production traits and immunity[J]. Poultry Science, 2003, 82(8): 1319-1325.

[101] WILLIAMS B A, VERSTEGEN M W A, TAMMINGA S. Fermentation in the monogastric large intestine: its relation to animal health[J]. Nutrition Research Reviews, 2001, 14: 207-227.

[102] CAINE W R, SAUER C W, HE J. Prebiotics, probiotics and egg yolk antibodies: novel alternatives to antibiotics for improving health of piglets and growing pigs[C]//Proceedings of the 10th International Symposium on Animal Nutrition. Kaposvár: Hungary, 2001: 33-53.

[103] YANG Y, IJI P A, KOCHER A, et al. Effects of dietary mannanoligosaccharide on growth performance, nutrient digestibility and gut development of broilers given different cereal-based diets[J]. Journal of Animal Physiology and Animal Nutrition, 2008, 92(6): 650-659.

[104] BAURHOO B, FERKET P R, ZHAO X. Effects of diets containing different concentrations of mannanoligosaccharide or antibiotics on growth performance, intestinal development, cecal and litter microbial populations, and carcass parameters of broilers[J]. Poultry Science, 2009, 88(11): 2262-2272.

[105] IANNACCONE F, BOVERA F. Mannanoligosaccharides in rabbit nutrition: a review[J]. Journal of Nutritional Ecology and Food Research, 2013, 1(1): 2-11.

[106] AZARAKHSH Y, SABOKBAR A, BAYAT M. The frequency of the most potentially toxigenic fungi in broiler feeds in Kermanshah province, west of Iran[J]. American-Eurasian Journal of Toxicological Sciences, 2011, 3: 11-16.

[107] RAUBER R H, DILKIN P, GIACOMINI L Z, et al. Performance of turkey poults fed different doses of aflatoxins in the diet[J]. Poultry Science, 2007, 86(8): 1620-1624.

[108] AWAD W A, BÖHM J, RAZZAZI-FAZELI E, et al. Effects of deoxynivalenol on general performance and electrophysiological properties of intestinal mucosa of broiler chickens[J]. Poultry Science, 2004, 83(12): 1964-1972.

[109] 吴峰洋, 李冲, 崔嘉, 等. 甘露寡糖对兔肠道健康及功能形态的影响[J]. 家畜生态学报, 2017, 38(6): 5-7, 36.

[110] JAHANIAN E, MAHDAVI A H, ASGARY S, et al. Effect of dietary supplementation of mannanoligosac-

charides on growth performance, ileal microbial counts, and jejunal morphology in broiler chicks exposed to aflatoxins [J]. Livestock Science, 2016, 190:123-130.

[111] WU L, LIAO P, HE L Q, et al. Growth performance, serum biochemical profile, jejunal morphology, and the expression of nutrients transporter genes in deoxynivalenol (DON)-challenged growing pigs [J]. BMC Veterinary Research, 2015, 11:144.

[112] ZAGHINI A, MARTELLI G, RONCADA P, et al. Mannanoligosaccharides and aflatoxin B1 in feed for laying hens: effects on egg quality, aflatoxins B1 and M1 residues in eggs, and aflatoxin B1 levels in liver [J]. Poultry Science, 2005, 84(6): 825-832.

[113] JOUANY J P, YIANNIKOURIS A, BERTIN G. The chemical bonds between mycotoxins and cell wall components of *Saccharomyces cerevisiae* have been identified [J]. Archiva Zootechnica, 2005, 8: 26-50.

[114] AWAAD M H H, ATTA A M, EL-GHANY W A, et al. Effect of a specific combination of mannan-oligosaccharides and β-glucans extracted from yeast cell wall on the health status and growth performance of ochratoxicated broiler chickens [J]. Journal of American Science, 2011, 7: 82-96.

[115] GHASEMIAN M, JAHANIAN R. Dietary mannan-oligosaccharides supplementation could affect performance, immunocompetence, serum lipid metabolites, intestinal bacterial populations, and ileal nutrient digestibility in aged laying hens [J]. Animal Feed Science and Technology, 2016, 213: 81-89.

[116] SHANMUGASUNDARAM R, SIFRI M, SELVARAJ R K. Effect of yeast cell product supplementation on broiler cecal microflora species and immune responses during an experimental coccidial infection [J]. Poultry Science, 2013, 92(5): 1195-1201.

[117] SHANMUGASUNDARAM R, SIFRI M, SELVARAJ R K. Effect of yeast cell product (CitriStim) supplementation on broiler performance and intestinal immune cell parameters during an experimental coccidial infection [J]. Poultry Science, 2013, 92(2): 358-363.

Research Advances in Regulatory Mechanism of Mannan-Oligosaccharides on Gut Health of Young Animals

CHAO Hongyu[1] YANG Yan[2] JIN Taihua[1] LYU Shenjin[1*]

(1. *College of Agriculture and Forestry Science, Linyi University, Linyi* 276003, *China*; 2. *Institute of Animal Science, Linyi Academy of Agricultural Sciences, Linyi* 276003, *China*)

Abstract: Mannan-oligosaccharides (MOS) is a mannose oligomer linked mainly by α-1,6 and α-1,2 glycosidic bonds. As a natural nutritional supplement, MOS is considered to produce a beneficial impact on young animal gut health through several mechanisms, including maintenance of gut micro-ecology balance, enhancement of intestinal mucosal barrier and immune functions, modulation of intestinal inflammation, promotion of early enterocyte development, and alleviation of the harmful effect of mycotoxins and coccidiosis, so it is often referred to as a potential alternative to antibiotic growth promoters in future animal breeding. In order to provide theoretical basis for further research and application of MOS, research advances of MOS in the mechanism of regulation on gut health of young animals and future research directions are summarized in this review. [***Chinese Journal of Animal Nutrition*, 2019, 31(10): 4411-4420**]

Key words: mannan-oligosaccharides; young animals; micro-ecology balance; immune enhancement; gut health

* Corresponding author, professor, E-mail: lvshenjin@lyu.edu.cn

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