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在线全文

自制肠内营养液增稠剂的热稳定性及吞咽安全性探索*

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【摘要】 目的 通过实验验证一种自制热稳定性增稠剂对于标准浓度的肠内营养液质构特性的影响，以及其在改善吞咽障碍方面的应用效果。**方法** ①取不同剂量梯度自制增稠剂（1.0 g、1.5 g、2.0 g、2.5 g、3.0 g）及常见的3种市售增稠剂，所有增稠剂中均加入23.391 g某款全营养配方粉溶于85 mL纯水，各配成100 mL标准浓度营养液。使用质构仪测量在不同温度梯度下（20 ℃、40 ℃、60 ℃、80 ℃）4种增稠后营养液的质构参数（内聚性、黏性、稠度、硬度），比较其热稳定性。②通过会厌切除术制造吞咽障碍大鼠模型，探究该增稠剂对吞咽障碍大鼠肺部组织损伤评分和炎性因子水平。取吞咽障碍大鼠模型分为待测干预组、阳性对照组、阴性对照组，并设立空白对照组（不进行手术，禁食1 d后正常饲养），每组15只。大鼠术后均禁食1 d后，待测干预组喂食自制增稠剂增稠的标准浓度营养液，阳性对照组喂食市售品3增稠的标准浓度营养液，阴性对照组正常饲养。4组均持续喂养2周，食物均加入食品级果绿色素。观察大鼠一般情况并记录体质量与食量。两周后，称重计算肺组织脏器系数，以常规HE染色评估脏器情况，根据Mikawa表评分计算肺组织损伤病理评分；收集血液上清检测血清总蛋白、白蛋白检测大鼠营养状况；实时定量聚合酶链反应（RT-qPCR）法检测肺组织中的白细胞介素-6（*IL*-6）、肿瘤坏死因子-α（*TNF*-*α*）基因表达；ELISA法检测肺组织、肺组织混悬液和血清中的IL-6、TNF-α蛋白表达；计算误吸发生率。**结果** ①在1.0～3.0 g的剂量范围内，20～80 ℃下，自制增稠剂增稠后的待测样品内聚性的热稳定性优于3种市售品，差异有统计学意义（P<0.01），黏性、硬度的热稳定性与3种市售品的差异无统计学意义。市售品1稠度热稳定性最优，待测样品和市售品2次之，市售品3最差，差异有统计学意义（P<0.01）。②动物实验结果示，阳性对照组和待测干预组体质量增加量低于空白对照组和阴性对照组（P<0.01）。待测干预组的脾脏系数低于阳性对照组和空白对照组（P<0.01），心脏、肝脏、肾脏系数低于空白对照组（P<0.01），肺脏系数与其他3组差异无统计学意义。待测干预组、阳性对照组和阴性对照组血清总蛋白、白蛋白水平均低于空白对照组（P<0.01）。ELISA检测结果示空白对照组和待测干预组血清中IL-6水平均低于阴性对照组和阳性对照组（P<0.05），其余指标4组间差异无统计学意义（P>0.05）。4组间肺组织损伤病理评分，肺组织中的*IL*-6、*TNF*-*α*基因表达水平的差异均无统计学意义。4组误吸发生率均为0。**结论** 自制肠内营养液增稠剂热稳定性优良，且符合吞咽安全性，可进一步探索其用于吞咽障碍患者的可行性。

【关键词】 复配增稠剂 质构特性 吞咽障碍 热稳定性 吞咽安全性

Examination of the Thermal Stability and Swallowing Safety of a Self-Developed Enteral Nutrition Thickening Agent

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【Abstract】 Objective To experimentally validate the effects of a self-developed heat-stable thickening agent on the textual characteristics of enteral nutrition solutions of standard concentration and its applicability in improving dysphagia. **Methods** A gradient of different doses of the self-developed thickening agent (1.0 g, 1.5 g, 2.0 g, 2.5 g, and 3.0 g) and three commonly used commercial thickeners were mixed with 23.391 g of a complete nutrition formula powder dissolved in 85 mL of purified water to prepare 100 mL standard concentration nutrition solutions. The textual parameters (cohesiveness, viscosity, thickness, and hardness) of these nutrition solutions were measured using a texture analyzer at various temperature gradients (20 ℃, 40 ℃, 60 ℃, and 80 ℃) to compare their thermal stability. A dysphagia rat model was created via epiglottectomy to explore the effects of the thickener on lung tissue damage scores and levels of inflammatory markers. The rats were divided into a test intervention group, a positive control group, a negative control group, and a blank control group (no surgery and normal feeding after fasting for one day), with 15 rats in each group. After fasting for one day post-surgery, the test intervention group was fed with the standard concentration nutrition solution thickened with the self-developed thickener, while the positive control group was given a standard concentration nutrition solution thickened with product 3, and the negative control group was fed a normal diet. All groups were fed for two weeks with food dyed with food-grade green dye. General conditions, body mass, and food intake were observed and recorded. After two weeks, abdominal aorta blood was collected, and heart, liver, spleen, lung, and kidney tissues were

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harvested and weighed to calculate the lung tissue organ coefficient. The organ conditions were evaluated using routine H&E staining, and lung damage was semi-quantitatively analyzed based on the Mikawa scoring criteria. Blood supernatants were collected to measure the total serum protein and albumin levels to determine the nutritional status of the rats. The expression of *IL-6* and *TNF-α* genes in lung tissues was measured by RT-qPCR. IL-6 and TNF-α protein expression levels in lung tissues, lung tissue homogenate, and serum were measured by ELISA. The aspiration incidence rate was calculated. **Results** Within the dosage range of 1.0 g to 3.0 g, the self-developed thickener in the test samples exhibited superior thermal stability in cohesiveness compared to the three commercially available thickeners, with a statistically significant difference (P<0.01). The differences in the thermal stability of viscosity and hardness between the self-developed thickener and the three commercially available thickeners were not statistically significant. The viscosity stability was optimal for the self-developed thickener, followed by the commercially available thickeners 1 and 3, with thickeners 2 being the least stable, though the differences were not statistically significant (P>0.05). Product 1 showed the best thermal stability in thickness, followed by the self-developed thickener and product 2, while the product 3 exhibited the worst performance, with the difference being statistically significant (P<0.01). The self-developed thickener had the best thermal stability in hardness at temperatures ranging from 20℃ to 80 ℃, followed by products 1 and 2, with product 3 being the least stable. However, the differences were not statistically significant (P>0.05). Animal experiment results indicated that the body weight gain in the positive control group and the test intervention group was lower than that in the blank and negative control groups (P<0.01). The spleen coefficient of the intervention group was lower than that of the positive control group and the blank control group (P<0.01), while the heart, liver, and kidney coefficients were lower than those of the blank control group (P<0.01). The differences in the lung coefficient of the intervention group and those of the other three groups were no statistically significant. Levels of TP and ALB in the test intervention group, the positive control group, and the negative control group were all lower than those in the blank control group, with statistically significant differences (P<0.01). ELISA results showed that serum IL-6 levels in the blank and test intervention groups were lower than those in the negative and positive control groups (P<0.05), while the difference in the other indicators across the four groups were not statistically significant (P>0.05). There were no statistically significant differences among the four groups in terms of lung tissue damage pathology scores, or in the levels of *IL-6* and *TNF-α* gene expression in lung tissues. The aspiration incidence rate was 0% in all groups. **Conclusion** The self-developed enteral nutrition thickening agent demonstrated excellent thermal stability and swallowing safety. Further research to explore its application in patients with dysphagia is warranted.

【Key words】 Composite thickener Textual characteristics Dysphagia Heat stability Swallowing safety

吞咽障碍是现临床上常见问题且逐渐引起广泛关注及重视,可由多种因素导致,如神经系统疾病、头颈部手术或老年人的生理性退化等[1]。吞咽障碍会导致食物摄入不足,严重影响患者的营养状态和生活质量[2]。增稠剂的使用已成为改善这一问题的有效手段[3]。其可改变食物或饮料的质构,以适应患者的吞咽能力,从而提高食物摄入量,改善营养状态[4]。然而,现市售增稠剂品类多,但国内市场份额多被国外产品占据[5],国外增稠剂不仅价格均较昂贵,且并未注重增稠剂的热稳定性[6]。我国是以热食为主的国家,吞咽障碍的老年人患者占比较大,多偏爱热食,因此我国需重视适合我国吞咽障碍患者的增稠食品领域的开发,研发具良好质构特性和热稳定性的增稠剂显得尤为重要[7]。标准浓度增稠营养液的吞咽的特性指标最佳。本研究通过实验验证一种自制热稳定性增稠剂对于标准浓度的肠内营养液质构特性的影响,以及其在改善吞咽障碍方面的应用效果。本研究旨在为吞咽障碍患者提供更安全、有效的辅助食品,同时为市售增稠剂提供新的替代选择。

1 材料与方法

1.1 实验材料

自制热稳定性增稠剂:配方为50%黄原胶:中轩生化、49%刺云实胶:山东齐鲁生物科技、1%糊精。市售增稠剂:市售品1(阶段Ⅰ、阶段Ⅱ、阶段Ⅲ):日本NUTRI,市售品2(薄稠、中稠、浓稠):日本healthy food笑容株式会社,市售品3(微稠、轻稠、中稠和浓稠):瑞士雀巢均按照商品使用说明进行配制(见表1)。某款全营养配方粉:含麦芽糊精、菊粉、低聚果糖、大豆分离蛋白等(Abbott)。

1.2 实验动物

60只雄性SPF级Sprague-Dawley(SD)大鼠,8周龄,体质量270 ~ 300 g,购买于浙江维通利华,饲养在四川省疾病预防控制中心实验动物房。实验获得四川大学华西医

表 1　市售增稠剂比较表

Table 1　Comparison of commercially available thickeners

Commercial product	Main Ingredients	Usage Instructions
Product 1	Maltodextrin and xanthan gum	Stage Ⅰ, Ⅱ, and Ⅲ dosage: 1.0 g, 2.0 g, and 3.0 g
Product 2	Guar gum and tapioca starch	Thin, medium, and thick consistency dosage: 0.7 g, 1.2 g, 1.7 g
Product 3	Hydroxypropyl distarch phosphate (modified corn starch)	Slight, light, medium, and thick consistency dosage: 1.02 g, 2.04 g, 3.06 g, 4.08 g

院实验动物伦理委员会批准(伦理备案号: 20211187A)。

1.3　实验方法

1.3.1　不同温度梯度下增稠剂质构测试

将不同剂量的各种增稠剂与营养粉混匀后, 加入沸水搅拌均匀, 然后待冷却至室温后, 在20 ℃、40 ℃、60 ℃、80 ℃温度梯度下分别用质构仪检测内聚性、黏性、稠度、硬度4个指标(具体见1.3.2), 其中, 40 ℃、60 ℃、80 ℃的样品是在相应温度水浴锅水浴5 min后上机测试, 每种待测品重复3个样本。3种市售品为对照组, 所有样品中均加入23.391 g某款全营养配方粉溶于85 mL纯水配成的100 mL标准浓度营养液。测试时质构仪参数具体设置如下: 方法类型选用Basic Single Test; 测试模式设置为Compression, 即压缩测试; 目标模式被设定为Distance, 即以距离为目标, 其目标值设定为3.000 mm; 测试前、测试进行时以及测试后的速度均被设置为0.50 mm/s; 触发模式选择为Force, 即力触发模式, 其触发点设定为3.000 gf。最后, 停止采集点被设定为起始位置。

1.3.2　评价指标

本研究者前期研究发现, 在20 ℃的室温条件下, 1.0 g、1.5 g、2.0 g、2.5 g、3.0 g待测增稠剂增稠后的营养液, 其内聚性范围能覆盖并且对标不同剂量市售增稠剂增稠厚的营养液(表1), 它们在不同温度梯度下(20 ℃、40 ℃、60 ℃、80 ℃)的内聚性、黏性、稠度、硬度, 则是本次研究的评价指标。

1.3.2.1　内聚性

内聚性是吞咽障碍患者食物最重要的指标之一, 内聚性越大, 食团分散性和流动性越小, 越不易分散进入气管引发吸入性肺炎, 越能降低吞咽风险, 因此研究以内聚性作为首要分析指标。内聚性指标的单位为mm, 反映了本研究使用质构仪测量中物理距离的变化, 提供了一种直观的方式来衡量样品内部粒子间相互作用的程度。这种测量反映了物质内部的凝聚力, 即物质部分之间抵抗被拉伸或分离的能力。

在本研究中, 对同一样品在某2个温度(即1个温度对, Pair)下的内聚性指标进行方差分析。若差异有统计学意义(即$P<0.05$), 则这种温度对($Pair_x$)表明在这2个温度下样品的内聚性存在显著差异(例如, 如果在20 ℃和40 ℃下市售品1的内聚性差异有统计学意义, 这被视为“1对”显著差异)。相反, 若差异无统计学意义(即$P>0.05$), 则这种温度对($Pair_y$)表明在这2个温度下样品的内聚性没有显著差异。$Pair_x$的数量与$Pair_y$的数量之和为总温度对数($Pair_t$)。通过计算$Pair_x$占$Pair_t$的比例($Pair_x$%), 可以评估样品内聚性的热稳定性。$Pair_x$%越高, 表明此样品内聚性的热稳定性越差。这种方法允许通过方差分析比较在不同剂量梯度的样品与各阶段市售品之间的内聚性大小。

1.3.2.2　黏性

黏性指标的单位为克力(gf), 该指标在一定程度上反映受试物黏附在口腔、咽部及食管的情况, 黏性越大, 受试物越容易残留在上述部位, 增加误吸的可能性, 同时也会给食用者带来不悦的体感, 因此将黏性作为第二重要的指标进行析。

计算$Pair_x$%, $Pair_x$%越高, 则此样品黏性的热稳定性越差。

1.3.2.3　稠度

稠度指标的单位为克力·秒(gf·s), 是反映食物流动性的指标之一, 稠度越大, 流动性越小, 食团流动速度越慢, 能有效降低吞咽安全风险。计算$Pair_x$%, $Pair_x$%越高, 则此样品稠度的热稳定性越差。

1.3.2.4　硬度

硬度指标的单位为gf, 是反映食物口感的一个指标, 由于本部分研究首要考虑的是食团吞咽的安全性, 因此将硬度放在最后分析。计算$Pair_x$%, $Pair_x$%越高, 则此样品硬度的热稳定性越差。

1.3.3　动物实验

ARRIVE(动物研究: 体内实验报告)指南[8]已明确要求动物实验报告解释实验动物所需样本量如何确定, 一般检测组织或体液中的生化或分子指标时, 建议每组大鼠数最好在8 ~ 12只或以上。本研究采用每组15只大鼠, 共设4个组, 分为待测干预组、阳性对照组、阴性对照组和空白对照组。除空白对照组外, 其余大鼠都进行会厌切除术。术后禁食1 d, 后对待测干预组喂食自制热稳定

增稠剂增稠后营养液,阳性对照组喂食市售品3增稠后营养液,阴性对照组和空白对照组正常饲养,均持续喂养2周。每周测量大鼠体质量1次。考虑到大鼠进食习惯为颗粒状饲料,自制增稠剂和市售品3按照推荐最大剂量给予,以达到最大黏稠度,接近饲料硬度,每只平均喂食35 g/d。食物均加入食品级果绿色素。观察大鼠一般情况并记录体重与食量。

两周后,取腹主动脉血后处死并收集心、肝、脾、肺、肾组织,固定24 h后包埋切片。以常规HE染色评估脏器情况,根据Mikawa表评分标准半定量分析肺损伤程度;收集血液上清检测血清总蛋白(total protein, TP)、白蛋白(albumin, ALB)以反映大鼠营养状况;实时定量聚合酶链反应(RT-qPCR)法检测肺部组织中的白细胞介素-6(*IL*-6)、肿瘤坏死因子-α(*TNF*-α)基因表达(见1.3.4),ELISA法(ELISA试剂盒:杭州联科生物有限公司)检测肺组织、肺组织混悬液和血清中的IL-6、TNF-α蛋白表达;计算误吸发生率(见1.3.5)。主要结局指标为IL-6和TNF-α蛋白的表达。

1.3.4 RT-qPCR法检测*IL*-6、*TNF*-α基因的表达

取20 mg肺部组织,使用MP裂解介质A管进行裂解,提取RNA,逆转录合成cDNA,使用SsoFast EvaGreen Supermix(Bio-rad)按照制造商的说明书进行RT-qPCR反应。其中*IL*-6正向引物序列5'-AGTTGCCTTCTTGGGACTGA-3',反向引物序列5'-TCCACGATTTCCCAGAGAAC-3'扩增产物长度142 bp;*TNF*-α正向引物序列5'-AGGCACTCCCCCAAAAGATG-3',反向引物序列:5'-TGAGGGTCTGGGCCATAGAA-3',扩增产物长度156 bp;*GAPDH*(内参基因)正向引物序列5'-TGGCCTTCCGTGTTCCTAC-3',反向引物序列5'-GAGTTGCTGTTGAAGTCGCA-3',扩增产物长度138 bp。采用$2^{-\Delta Ct}$计算每组、每个样本目的基因相对内参基因的表达量。

1.3.5 误吸发生率

观察肺部组织、肺部组织混悬液以及混悬液离心后的上清液和沉淀的颜色,出现绿色即记为误吸发生。误吸发生率的计算公式为

$$\text{误吸发生率} = \frac{\text{每组发生误吸的大鼠数量}}{\text{每组大鼠数量}} \quad (1)$$

1.3.6 脏器系数和肺组织损伤评分

主要脏器质量指心脏、肝脏、脾脏、肺和肾脏的质量,直接称量获得。脏器系数是指某一脏器的重量与体重或体表面积之比,用来评估脏器的肥大或萎缩。

$$\text{脏器系数} = \frac{\text{大鼠脏器质量}}{\text{大鼠体质量}} \quad (2)$$

上式中的质量单位均为g。

肺部组织损伤评分:通过组织病理学的评分来判断,研究采用 Mikawa表评分标准,检查项目包括肺泡充血、肺组织出血、腔隙或血管壁中性粒细胞浸润/聚集、肺泡壁厚度或者透明膜形成肺泡充血,0 ~ 4分分别代表几乎无损伤、轻微损伤、中度损伤、严重损伤和最大损伤。

1.3.7 营养状况

取100 μL血清样品,比氏蛋白定量法检测TP,布里斯绿色染料结合法检测ALB。

1.4 统计学方法

计量资料用均数$\bar{x} \pm s$描述,计数资料采用频数(百分率)表示,用SPSS 22软件进行统计学分析,用Origin 2021和 Graphpad Prism 7软件进行绘图。剔除异常值后计量资料采用单因素方差分析,事后检验采用LSD检验,计数资料采用卡方检验和Fisher确切概率法。$P \leqslant 0.05$为差异有统计学意义。

2 结果

2.1 各受试样品在不同温度下内聚性、黏性、稠度、硬度的热稳定性

与市售品相比,待测样品在各温度点的内聚性与市售品1差异无统计学意义($P > 0.05$),而优于市售品2($P < 0.01$)和市售品3($P < 0.01$)。待测样品在不同温度下内聚性差异性最小(0%),市售品1(16.7%)和市售品3(27.8%)次之,市售品1(29.2%)最差,经卡方检验差异有统计学意义($P < 0.01$)。

与市售品相比,待测样品在各温度点的黏性表现与市售品1相似($P > 0.05$),而优于市售品2($P < 0.01$)和市售品3($P < 0.01$)。待测样品在不同温度下黏性差异性最小(13.3%),市售品1(16.7%)和市售品3(37.5%)次之,市售品2(38.9%)最差,经卡方检验差异无统计学意义($P > 0.05$)。

与市售品相比,待测样品在各温度下的稠度表现与市售品1和市售品2相似,差异无统计学意义($P > 0.05$),而优于市售品3($P < 0.01$)。市售品1在不同温度下稠度差异性最小(0.0%),待测样品(13.3%)和市售品2(38.9%)次之,市售品3(50.0%)最差,经卡方检验差异有统计学意义($P < 0.01$)。

与市售品相比,待测样品在各温度下的稠度与市售品1差异无统计学意义($P > 0.05$),而优于市售品2($P < 0.01$)和市售品3($P < 0.01$)。待测样品在不同温度下硬度差异性最小(13.3%),市售品1(27.8%)和市售品2(33.3%)次之,市售品3(45.8%)最差,经卡方检验差异无统计学意义($P > 0.05$)。表2。

2.2　增稠营养液饲养后大鼠一般状况与体质量变化

术后禁食1 d后进食。阳性对照组与待测干预组各有1只大鼠在术后早期死亡。空白对照组状态正常，其余三组大鼠出现活动性降低、咳嗽、呼吸困难等症状，同时饮水减少、排泄物软化。术后1周，阳性对照组和待测干预组大鼠体质量增加量低于空白对照组和阴性对照组（$P<0.01$）。术后2周，3组模型鼠的体质量增加量均小于空白对照组（$P<0.01$），阳性对照组和待测干预组大鼠之间体质量增加量差异无统计学意义（$P>0.05$）。见图1。

表 2　各受试样品在不同温度下内聚性、黏性、稠度、硬度的热稳定性

Table 2　Thermal stability of cohesiveness, viscosity, thickness, and hardness of each test sample at different temperatures

Group	Pair$_t$/pair	Pair$_x$ (Pair$_x$%)/pair (%)			
		Cohesiveness$^{\#}$	Viscosity	Consistency$^{\#}$	Hardness
Test sample	30	0 (0)	4 (13.3)	4 (13.3)	4 (13.3)
Commercial product 1	18	3 (16.7)	3 (16.7)	0 (0)	5 (27.8)
Commercial product 2	18	5 (27.8)*	7 (38.9)*	7 (38.9)*	6 (33.3)*
Commercial product 3	24	7 (29.2)*	9 (37.5)*	12 (50.0)*	11 (45.8)*

In this study, the cohesion index of the same sample under 2 certain temperatures (i.e., 1 temperature pair) was analyzed by variance. If the difference is statistically significant (i.e., $P<0.05$), then this temperature pair (Pair$_x$) show a significant difference in the cohesion of the sample at these two temperatures (for example, if there is a statistically significant difference in the cohesion of commercial product 1 at 20 ℃ and 40 ℃, this is considered "1 pair" of significant difference). Conversely, if the difference is not statistically significant (i.e. $P>0.05$), the temperature pair (Pair$_y$) indicates that there is no significant difference in sample cohesion at the two temperatures. The sum of the number of Pair$_x$ and the number of Pair$_y$ is the total temperature logarithm (Pair$_t$). By calculating the proportion of Pair$_x$ to Pair$_t$ (Pair$_x$%), the thermal stability of sample cohesion can be assessed. The higher the Pair$_x$%, the worse the thermal stability of the sample cohesion. This method allows the comparison of the cohesiveness between samples at different dose gradients and commercially available products at various stages by ANOVA. The evaluation methods for viscosity, consistency, and hardness are similar. The higher Pair$_x$% is, the worse the thermal stability of viscosity, consistency, and hardness are.* Data pairs showing statistically significant differences in ANOVA analysis.$^{\#}$ $P<0.01$ among the groups (Chi-square test).

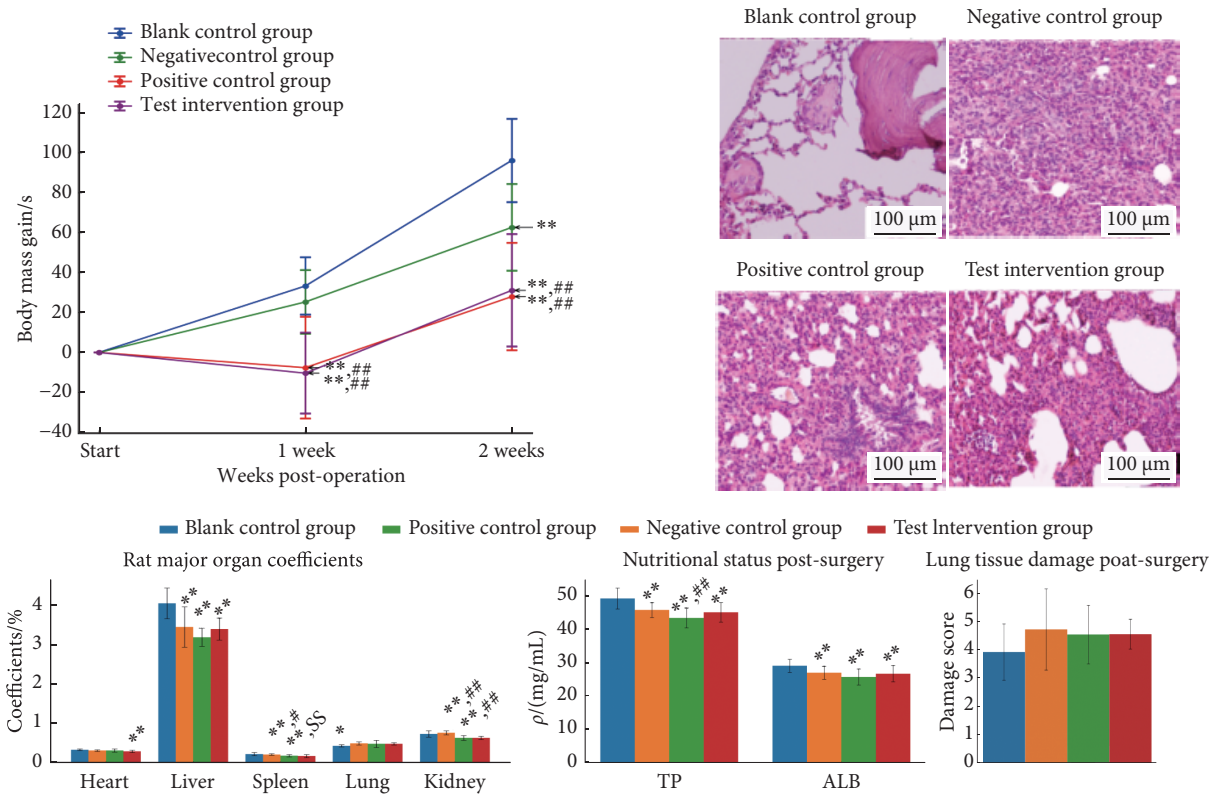

图 1　增稠营养液喂养后2周大鼠体质量增加量变化、脏器系数、营养、肺部组织损伤和肺部组织HE染色结果

Fig 1　Changes in body mass gain, organ coefficient, nutrition, lung tissue injury, and H&E staining results of lung tissues in rats fed with thickened nutrient solution for 2 weeks

$^{*}P<0.05$, $^{**}P<0.01$, vs. blank control group; $^{\#}P<0.05$, $^{\#\#}P<0.01$, vs. negative control group; $^{SS}P<0.01$, vs. positive control group. n=14 in the positive control group and the test lntervention group and n=15 in the blank control group and the negative control group.

2.3 增稠营养液饲养2周后大鼠脏器、营养和肺部组织损伤情况

见图1。空白对照组心脏系数高于待测干预组，肺脏系数低于阴性对照组，脾脏系数和肾脏系数高于待测干预组和阳性对照组，肝脏系数高于其余3组，差异均有统计学意义（$P<0.01$或$P<0.05$）。待测干预组的脾脏系数低于阳性对照组和空白对照组（$P<0.01$），心脏、肝脏、肾脏系数低于空白对照组（$P<0.01$），肺脏系数与其他3组差异无统计学意义。空白对照组血清中TP和ALB水平均高于其他3组（$P<0.01$）；阳性对照组TP水平低于阴性对照组（$P<0.01$），ALB水平差异无统计学意义（$P>0.05$）。肺组织损伤评分4组间差异无统计学意义（$P>0.05$）。空白对照组呈现肺泡轻度充血和局部出血；阴性对照组和阳性对照组出现肺泡轻中度充血，大量中细粒细胞浸润和局部轻中度出血，疑似有透明膜形成；待测干预组染色结果与阴（阳）性对照组接近，但无透明膜形成。

2.4 大鼠IL-6、TNF-α的基因和蛋白表达水平

见图2、表3。RT-qPCR检测结果显示，空白对照组大鼠肺组织*IL-6*、*TNF-α*基因表达水平最低，其次为待测干预组和阳性对照组，阴性对照组表达水平最高，但4组间差异无统计学意义。ELISA法检测结果显示，空白对照组和待测干预组血清中IL-6水平均低于阴性对照组和阳性对照组（$P<0.05$），血清中的TNF-α，肺组织混悬液的IL-6、TNF-α，这3个指标在4组间差异无统计学意义。

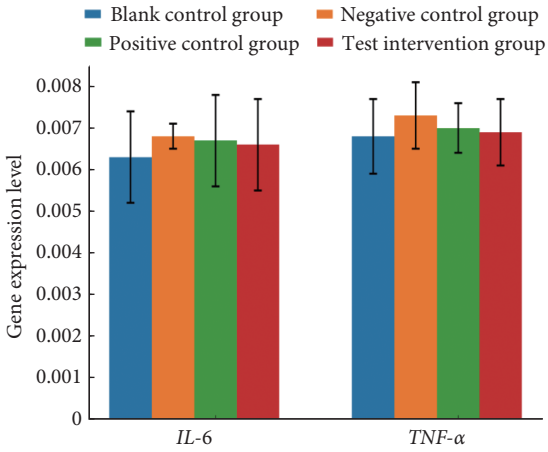

图 2 增稠营养液喂养后2周大鼠肺组织中*IL-6*、*TNF-α*基因的表达

Fig 2 Gene expression of *IL-6* and *TNF-α* in lung tissue in rats fed with thickened nutrient solution for 2 weeks

n=14 in the positive control group and the test lntervention group and *n*=15 in the blank control group and the negative control group.

表 3 增稠营养液喂养后2周大鼠肺组织混悬液、血清中IL-6、TNF-α蛋白表达

Table 3 Expression of IL-6 and TNF-α proteins in lung tissue homogenate and serum in rats fed with thickened nutrient solution for 2 weeks

Index	Blank control group (*n*=15)	Negative control group (*n*=15)	Positive control group (*n*=14)	Test intervention group (*n*=14)
Lung tissue				
IL-6/(pg/mg)	15.85±4.03	18.48±4.75	18.24±7.44	17.26±6.53
TNF-α/(pg/mg)	39.83±9.32	41.60±10.58	40.87±10.51	40.54±17.21
Serum				
IL-6/(pg/mL)	21.72±6.03	27.69±7.69*	27.41±2.45*	21.61±7.29$^{\#,S}$
TNF-α/(pg/mL)	86.32±18.79	94.04±18.74	87.30±26.40	88.82±28.17

* $P<0.05$, vs. blank control group; $^{\#}$ $P<0.05$, vs. negative control group; ^{S} $P<0.05$, vs. positive control group.

2.5 增稠营养液喂养后2周大鼠误吸发生率

4组大鼠肺部组织、组织混悬液及离心后的上清液和沉淀依旧均无染色情况发生，误吸阳性率为0%。见图3。

3 讨论

本研究旨在探究自制增稠剂在不同温度梯度下（20 ℃、40 ℃、60 ℃、80 ℃）与现市售品的硬度、稠度、黏性和内聚性等比较，以此来评价该款自制增稠剂在加热状态下的热稳定性和吞咽特性。本研究自制增稠剂和三种市售品增稠后的营养液的吞咽特性都达到了日本通用设计食品（UDF）等国际公认的吞咽障碍食物质地标准[9]。研究结果提示：在四个温度下自制增稠剂具备良好的热稳定性，具体体现在其内聚性、稠度、黏性和硬度等质构指标差异性最小，且内聚性显著优于市售品；并且在内聚性无差异状态下，自制增稠剂的黏性、稠度和硬度较低，食团更易流动[10]。考虑自制增稠剂上述表现可能与其复配成分有关，其主要含有黄原胶、刺云实胶，而市售增稠剂成分为麦芽糊精、黄原胶、瓜尔胶、木薯淀粉和羟丙基二淀粉磷酸酯（变性玉米淀粉）。有研究发现木薯淀粉在热处理时表现出黏性行为，而羟丙基二淀粉磷酸酯和黄原胶增稠的基质在热处理时表现出弹性行为[11]。而黄原胶分子具有复杂的空间构型和交联结构，利于其在高温下维持其增稠功能[12]。刺云实胶分子中的侧链官能团能够与水分子形成水合壳，从而有助于在高温下维持其分子结构的稳定性[13]。因此，可认为该增稠剂具较好热稳定性，有作为吞咽障碍患者安全吞咽辅助产品的潜力和应用价值。本研究大鼠实验结果显示，喂饲增稠营养液的阳性干预组和待测干预组体质量增长量低于正常饲养

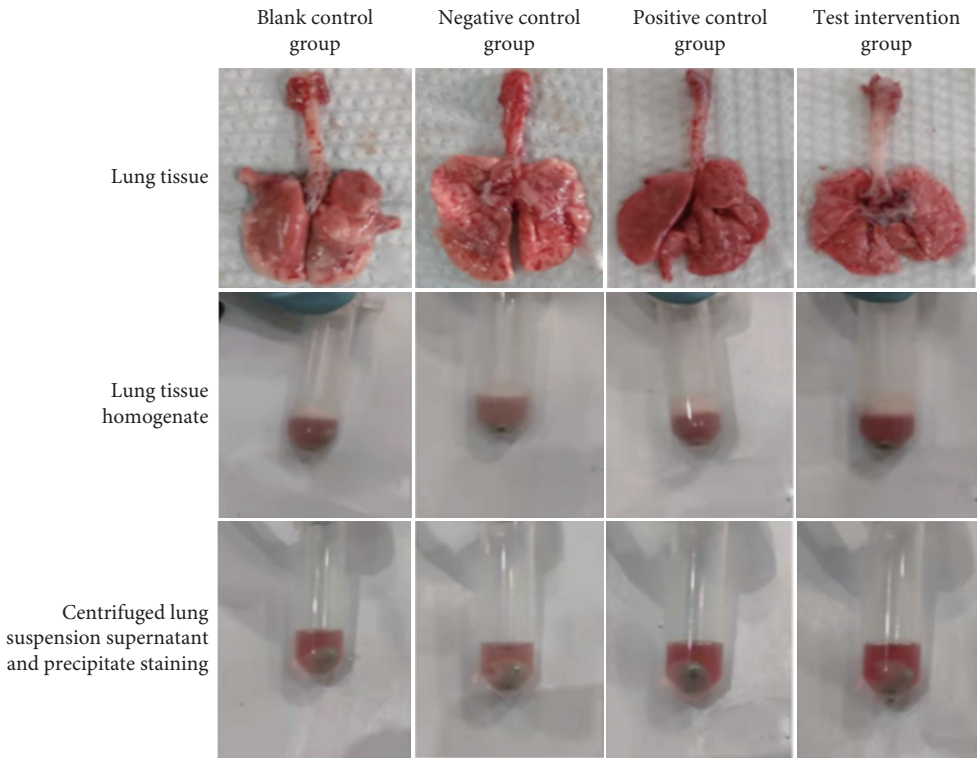

图 3 增稠营养液喂养后2周大鼠肺部组织染色情况

Fig 3 Postoperative lung tissue staining in rats fed with thickened nutrient solution for 2 weeks

的空白对照组和阴性对照组，营养指标TP和ALB水平也低于正常对照组，提示吞咽障碍与营养不良密切相关[14-15]。待测干预组、阳性对照组两组的肺组织脏器系数低于阴性对照组，表明自制增稠剂和市售品3具一定预防误吸的作用。在本研究中，选择炎症标志物IL-6和TNF-α作为吞咽安全性评估的主要结局指标，IL-6和TNF-α是促炎细胞因子，在多种炎症反应和组织损伤中起关键作用，高水平的IL-6和TNF-α可以为吞咽障碍引发误吸而造成的肺部炎症性损伤提供直接证据[16]。待测干预组的肺损伤评分及炎性因子水平均不劣于阳性对照组、阴性对照组和空白对照组，且其中个别指标（如待测干预组血清中IL-6水平）还优于阴性对照组和阳性对照组，表明待测干预组大鼠吞咽障碍相关指标具有好转趋势，且大鼠食用自制增稠剂增稠的营养液比食用市售品3增稠后营养液误吸的量更少，故而干预组炎症反应更弱，其炎症因子表达比阳性组低，也可证实自制增稠剂对于吞咽障碍患者具有辅助安全进食的功效。自制增稠剂和市售品3可提高吞咽安全，符合现有研究[17]。但关于吞咽安全性的探究，后续需利用VFSS等仪器设备进行吞咽障碍症状诊断，并进一步将该增稠剂应用到临床吞咽障碍患者观察。

总的来说本研究构建了一种新型的复配增稠剂，并证实具良好的吞咽特性和热稳定性，能有效调节营养液的质构和吞咽特性，优于市售的三种增稠剂，但其质构特性来满足吞咽障碍分级营养管理的研究和开发[18-20]，还需更多研究来探索。

*　　*　　*

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Author Contribution　CHEN Muxi is responsible for conceptualization, data curation, formal analysis, project administration, resources, supervision, visualization, writing--original draft, and writing--review and editing. SHANG Zhengyun is responsible for conceptualization, data curation, formal analysis, investigation, methodology, project administration, supervision, writing--original draft, and writing--review and editing. CHENG Yi is responsible for conceptualization, data curation, formal analysis, investigation, methodology, resources, software, writing--original draft, and writing--review and editing. LI Ke is responsible for funding acquisition. DUAN Feixia is responsible for funding acquisition and resources. HU Wen is responsible for conceptualization, funding acquisition, project administration, software, and validation. All authors consented to the submission of the article to the Journal. All authors approved the final version to be published and agreed to take responsibility for all aspects of the work.

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Declaration of Conflicting Interests All authors declare no competing interests.

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