7.1 Quality Management System Certification (ISO 13485)

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DAkkS Deutsche Akkreditierungsstelle D-ZM-11321-01-00

Product Service

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Facility(ies): **NMS Technologies Co., Ltd.**
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PEOPLE'S REPUBLIC OF CHINA

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Certification Mark:

Scope of Certificate: **Design and Development, Production and Distribution of Spray Dressing**

Applied Standard(s): ISO 13485:2016
(EN ISO 13485:2016/AC:2018, EN ISO 13485:2016/A11:2021)
Medical devices - Quality management systems - Requirements for regulatory purposes

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Report No.: SH23114601

Valid from: 2023-12-01
Valid until: 2026-11-30

Date, 2023-10-16

Christoph Dicks
Head of Certification/Notified Body

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7.3 Biocompatibility Evaluation (ISO 10993)

Test to be Performed (standard reference)	Extract(s) it used (polar,non-polar) or animal model/cell line	Extract conditions (time temp area or mass to volume ratio compared to in-use conditions)	Test and control(s) used	Pass/Fail Criteria (units when appropriate)
Cytotoxicity	1X Minimal Essential Media	ISO10993-5:1992 37 ℃ for 24hrs w/MEM	ISO10993-5:1992	Pass Lysis<70%
Sensitization (w/2 extracts)	Dimethylsulfoxide (DMSO)	ISO10993-10:1995 Mice (5 per extract) Reactions recorded at day 1 and day 6	ISO10993-10:1995	Pass Stimulation Index of less than 3.0
Irritation/ Intracutaneous Toxicity (w/2 extracts)	Sodium Chloride, Sesame Oil, NF Extract, Alcohol Saline, Polyethylene Glycol	ISO10993-10:1995 Rabbits (2 pair per extract) Reactions recorded at 24,48& 72 hrs	ISO10993-10:1995	Pass Primary Irritation Index (PII) of 0-1.9

Report Number 20020532-1

FINAL TEST REPORT

CYTOTOXICITY TEST – ISO 10993-5

(Agarose Overlay Method)

Test Article

Long-acting Antimicrobial Material

Final Report Date

August 06, 2002

MANAGEMENT OF THE STUDY

Performing Laboratory

Center of Medical Devices

National Institute for the Control of

Pharmaceutical and Biological Product,

Temple of Heaven,

Beijing 100050, China

Sponsor

Nanjing Magic Science and Technology Co., LTD

259 North Zhongshan Road,

Nanjing 210003, China

Report Number 20020532-2

FINAL TEST REPORT

KLIGMAN MAXIMIZATION TEST – ISO 10993-10

Test Article

Long-acting antimicrobial material

Final Report Date

August 06, 2002

MANAGEMENT OF THE STUDY

Performing Laboratory

Center of Medical Devices
National Institute for the Control of
Pharmaceutical and Biological Product,
Temple of Heaven,
Beijing 100050, China

Sponsor

Nanjing Magic Science and Technology Co., LTD
259 North Zhongshan Road,
Nanjing 210003, China

Report Number 20020532-3

FINAL TEST REPORT

SKIN IRRITATION TEST – ISO 10993-10

Test Article

Long-acting Antimicrobial Material

Final Report Date

August 06, 2002

MANAGEMENT OF THE STUDY

Performing Laboratory

Center of Medical Devices

National Institute for the Control of

Pharmaceutical and Biological Product,

Temple of Heaven,

Beijing 100050, China

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3.4 Independent Clinical Susceptibility Studies

"皮肤物理抗菌膜"与常用抗生素对临床耐药菌株药敏情况的比较研究

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【摘 要】 目的 研究物理抗菌方法(非药物)对常见临床耐药菌株的药敏情况。方法 对临床分离率>5%的无特殊营养需求的7种细菌,分离培养后,采用抗菌药物最低抑菌浓度(MIC)稀释法,比较常用抗生素及"皮肤物理抗菌膜"的耐药情况。结果 临床分离率>5%的7种细菌分别为:大肠埃希氏菌、金黄色葡萄球菌、铜绿假单胞菌、不动杆菌、肺炎克雷伯菌、产气肠杆菌、阴沟肠杆菌。大肠埃希氏菌对左氧氟沙星、氨苄西林、哌拉西林、庆大霉素、头孢唑林、头孢他啶的耐药率为12.2%~82.1%;肺炎克雷伯菌对上述6种抗生素的耐药率为13.4%~94.3%;产气肠杆菌对上述6种抗生素的耐药率为7.2%~79.3%;阴沟肠杆菌对上述6种抗生素的耐药率为28.1%~95.8%;铜绿假单胞菌对上述6种抗生素的耐药率为20.7%~100%;不动杆菌对上述6种抗生素的耐药率为21.3%~95.2%;耐甲氧西林金黄色葡萄球菌(MRSA)对青霉素、左氧沙星、氨苄西林、苯唑西林、哌拉西林、庆大霉素、头孢唑林、头孢他啶的耐药率为20.6%~100%;甲氧西林敏感的金黄色葡萄球菌(MSSA)对上述8种抗生素的耐药率分别为0.0%~85.8%;以上分离菌对"皮肤物理抗菌膜"洁悠神长效抗菌材料均敏感,耐药率为0。结论 "皮肤物理抗菌膜"具有广谱抗菌、敏感率高的特点,为临床治疗感染特别是多重耐药菌株的感染提供了高效的新型抗菌材料。

【关键词】 耐药菌株;"皮肤物理抗菌膜";药敏

中图分类号:R969.3 文献标识码:A doi:10.3969/j.issn.1002-1310.2011.03.002

A comparison study of susceptibility to clinical drug-resistant strains between skin physical antimicrobial film and common antibiotics

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【Abstract】Objective To investigate the innovative physical antimicrobial method's (non-drug) susceptibility to common clinical resistant strains. Methods After the isolated culture of 7 species of bacteria without any specific nutritional requirements whose clinical isolation rate was > 5%, the drug resistance of common antibiotics and "skin physical antimicrobial film" patent technology was compared by antibiotics minimum inhibitory concentration (MIC) dilution method. Results The isolated 7 species of bacteria with a clinical isolation rate of > 5% were Escherichia coli, Staphylococcus aureus, Pseudomonas aeruginosa, Acinetobacter, Klebsiella pneumoniae, Enterobacter aerogenes and Enterobacter cloacae. The resistance rate of Escherichia coli to Levofloxacin, ampicillin, piperacillin, gentamicin, cefazolin, ceftazidime was 12.2% ~82.1%; the resistance rate of Klebsiella pneumoniae to the above 6 kinds of antibiotics was 13.4% ~94.3%; the resistance rate of Aerogenes to the above 6 kinds of antibiotics was 7.2% ~79.3%; the resistance rate of Enterobacter cloacae to the above 6 kinds of antibiotics was 28.1% ~95.8%; the resistance rate of Pseudomonas aeruginosa to the above 6 kinds of antibiotics was 20.7% ~100%; the resistance rate of Acinetobacter to the above 6 kinds of antibiotics was 21.3% ~95.2%; the resistance rate of Methicillin-resistant Staphylococcus aureus (MRSA) to penicillin, levofloxacin, ampicillin, oxacillin, piperacillin, gentamicin, cefazolin, ceftazidime was 20.6% ~100%; the resistance rate of Methicillin-sensitive Staphylococcus aureus (MSSA) to the above 8 kinds of antibiotics was 0.0% ~85.8%; These isolates were susceptible to "skin physical antimicrobial film" patent technology product JUC long-lasting antimicrobial materials, and the drug resistance rate is 0. Conclusion "Skin physical antimicrobial film" patent technology has broad-spectrum antimicrobial function and high susceptiblity, providing a highly effective new antimicrobial material for the clinical treatment of infections, especially the infections of multi-drug resistant strain.

【Key word】 Resistant Strains; Skin physical antimicrobial film; Susceptibility; Antibiotics

抗生素是对细菌性感染治疗的首选药物,然而细菌对抗生素的耐药性正成为现代医学的重大威胁[1]。"皮肤物理抗菌膜"形成的纳米物理抗菌膜,提供了一种非药物的物理抗菌模式,为临床细菌性感染提供了一种新的解决方法。本研究通过对常用抗生素与"皮肤物理抗菌膜"洁悠神长效抗菌材料的药敏结果进行比较,以评价洁悠神的临床应用效果。

1 材料和方法

1.1 一般资料 所有样本来自本院烧伤科2001年5月至2003年1月间送检的创面分泌物标本,这些创面分泌物标本来自于42例烧伤患者,其中男25例,女17例,年龄7~69岁;烧伤面积5%~79%体表总面积(TBSA),平均烧伤面积25.3±7.5% TBSA。

1.2 菌株来源 从创面分泌物标本中共分离出315株无特殊要求的病原菌,临床分离率>5%的7种细菌分别为:大肠埃希氏菌、金黄色葡萄球菌、铜绿假单胞菌、不动杆菌、肺炎克雷伯菌、产气肠杆菌、阴沟肠杆菌。

1.3 常用抗生素和试剂 青霉素、左氧氟沙星、氨苄西林、苯唑西林、哌拉西林、庆大霉素、头孢唑林、头孢他啶;洁悠神长效抗菌材料。

1.4 方法

【收稿日期】2011-02-18 ※通讯作者

1.4.1 细菌鉴定 按常规培养方法[2],挑取典型菌落采用微生物半自动鉴定系统进行细菌鉴定。

1.4.2 药敏试验 抗生素与洁悠神长效抗菌材料敏感试验参照稀释法进行,耐药菌株结果参照NCCLS 1997[3]标准进行判断,根据耐药结果计算出耐药率。

1.4.3 药敏试验的质量控制 以大肠埃希氏菌ATCC 25922,金黄色葡萄球菌ACTT 25923,铜绿假单胞菌ATCC 27853作为质控菌株进行药敏试验的质控,结果均在NCCLS 1997规定的合格范围。

2 结 果

2.1 菌株分布 从临床标本中共分离出无特殊营养要求的细菌315株,分离率超过5%的7种细菌依次为:大肠埃希氏菌(16.9%)、金黄色葡萄球菌(15.8%)、铜绿假单胞菌(12.3%)、不动杆菌(9.4%)、肺炎克雷伯菌(8.6%)、产气肠杆菌(6.9%)、阴沟肠杆菌(6.4%),详细结果见表1。

表1 临床分离出的315株中分离率超过5%的7种细菌菌株分布表

菌 种	分离菌株数	分离率(%)
大肠埃希氏菌	53	16.9
金黄色葡萄球菌	50	15.8
铜绿假单胞菌	39	12.3
不动杆菌	30	9.4
肺炎克雷伯菌	27	8.6
产气肠杆菌	22	6.9
阴沟肠杆菌	20	6.4

2.2 抗生素的药敏分析 以分离率>5%的7种细菌为代表,根据NCCLS 1997标准对各属细菌中应首先选用的抗生素药敏结果及洁悠神的药敏结果进行了试验,计算出耐药率。结果见表2。

表2 各属主要细菌常用抗生素与洁悠神长效抗菌材料的耐药率(%)

抗生素	肠杆菌科				金黄色葡萄球菌		铜绿假单胞菌和不动杆菌属	
	大肠埃氏菌	肺炎克雷伯菌	产气肠杆菌	阴沟肠杆菌	MRSA	MSSA	铜绿假单胞菌	不动杆菌
青霉素					100.0	85.8		
左氧氟沙星	62.4	13.4	22.1	40.2	57.6	30.2	32.2	21.3
氨苄西林	82.1	94.3	76.5	95.8	90.5	48.6	99.6	55.9
苯唑西林	82.1	94.3	76.5	95.8	100.0	0.0		
哌拉西林	53.4	68.2	29.2	35.6	45.3	37.6	34.1	66.2
庆大霉素	42.9	18.9	7.2	28.1	65.8	25.12	53.6	47.9
头孢唑林	41.0	21.2	79.3	89.3	20.6	70.21	100.0	95.2
头孢他啶	12.2	19.5	30.6	62.3	74.7	11.6	20.7	52.7
洁悠神	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0

3 讨 论

随着对抗感染治疗的发展,越来越多的抗生素被应用到临床,虽然取得了很好的临床治疗效果,但是研究人员发现,细菌在多次与抗生素接触后,对药物的敏感性减少甚至消失,致使抗生素对耐药菌的疗效降低甚至无效[4]。耐药菌引发的感染导致更多疾病的发生、更长时间的治疗以及增加传染给其他人的威胁[5]。在减少耐药菌株的产生及控制耐药菌所致感染的过程中,合理应用抗菌药物及继续寻找治疗耐药菌所致感染的新的有效途径,仍是重要的措施之一。

"皮肤物理抗菌膜"为一种高分子活性剂,其水溶性制剂喷洒在皮肤、黏膜表面形成一层致密的正电荷网状膜;对带负电荷的细菌、真菌、病毒等病原微生物具有强力吸附作用,通过静电力作用达到杀灭或抑制病原微生物,不会产生耐药性[6]。经中国国家药监局(SFDA)批准为Ⅲ类医疗器械。适用于因病原微生物引起的炎症感染创面及物理、机械、热力因素引起的创面,以杀灭和隔离细菌、真菌及病毒。

通过我们的研究发现,临床常见致病菌依然是大肠埃希菌、金黄色葡萄球菌、铜绿假单胞菌等,与其它文献资料相同[7-9],其种类并未见明显改变,但对抗生素的敏感性与耐药性却发生了巨大变迁,有的菌株对某种抗生素的耐药率达到了100%。在试验过程中,我们惊喜的发现,分离出的菌株对"皮肤物理抗菌膜"洁悠神"长效抗菌材料均表现出高度敏感性。

"'皮肤物理抗菌膜'专利技术解决局部感染和院内感染方案"作为中国卫生部"十年百项"推广项目无疑为我们医生控制感染特别是多重耐药菌所致感染增加了新的物理抗菌武器,可替代抗生素用于感染治疗,并可避免耐药。本次研究为以后采用创新的"皮肤物理抗菌膜"专利技术进行其他耐药方面的研究奠定了基础。

物理抗微生物膜与常用抗菌药物对糖尿病足耐药菌株药敏情况的比较研究

梅清华　范翠琼　杨茵　李明友　林茂锐

【摘要】 **目的**　研究创新物理抗微生物膜对临床糖尿病足耐药菌株的药敏情况。**方法**　对168例糖尿病足感染患者行病原菌分离培养，以最低抑菌浓度（MIC）稀释法进行药敏试验，比较常用抗菌药物及物理抗微生物膜的耐药情况。**结果**　分离出的63株菌株按构成比例由多到少依次为：金黄色葡萄球菌、铜绿假单胞菌、产气肠杆菌、阴沟肠杆菌、不动杆菌、表皮葡萄球菌。金黄色葡萄球菌对青霉素、左氧氟沙星、氨苄西林、苯唑西林、哌拉西林、庆大霉素、头孢唑林、头孢他啶等8种抗菌药物耐药率为23.5%～100%；铜绿假单胞菌为23.5%～97.8%；产气肠杆菌为7.5%～75.3%；阴沟肠杆菌为30.5%～94.6%；不动杆菌为21.6%～94.6%；表皮葡萄球菌为5.6%～83.8%。以上6种分离菌对物理抗微生物膜耐药率为0。**结论**　物理抗微生物膜具有广谱抗菌，对各种细菌敏感率高的特点，为临床治疗糖尿病足提供了有效，而且可避免耐药的物理学抗感染新方法。

【关键词】　耐药菌；糖尿病足；药敏；物理抗微生物膜；抗菌药物

Comparative study on susceptibility of physical antimicrobial film and common antibiotics against drug-resistant strains isolated from diabetic foot

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【Abstract】 **Objective**　To study susceptibility of innovative physical method against resistant strains isolated from clinical diabetic foot. **Methods**　Pathogens from 168 cases of patients with diabetic foot infections were isolated and cultured, minimum inhibitory concentration (MIC) dilution method was adopted for susceptibility test to compare drug resistance of Physical Antimicrobial Film and common antibiotics. **Results**　63 strains were cultured and isolated from affected parts of diabetic foot patients. According to ratio, the strains from the maximum to minimum were: Staphylococcus aureus, Pseudomonas aeruginosa, Enterobacter aerogenes, Enterobacter cloacae, Acinetobacter, Staphylococcus epidermidis. The drug-resistant rates of Staphylococcus aureus to penicillin, levofloxacin, ampicillin, oxacillin, piperacillin, gentamicin, cefazolin, ceftazidime were 23.5% to 100%; those of Pseudomonas aeruginosa to eight antibiotics were 23.5% to 97.8%; those of Enterobacter aerogenes to eight antibiotics were 7.5% to 75.3%; those of Enterobacter cloacae to eight antibiotics were 30.5% to 94.6%; those of Acinetobacter to eight antibiotics were 21.6% to 94.6%; those of Staphylococcus epidermidis to eight antibiotics were 5.6% to 83.8%. The drug-resistant rates of the above six isolated strains to Physical Antimicrobial Film JUC Spray Dressing were 0. **Conclusion**　Physical Antimicrobial Film has the characteristics of broad-spectrum antimicrobe, with high sensitive rates to a variety of bacteria. It provides a new effective anti-infective physics (not chemical or biological) method and can avoid drug resistance for the clinical treatment of diabetic foot.

【Key words】 Drug-resistant strains; Diabetic foot; Susceptibility; Physical Antimicrobial Film; Antibiotics

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原微生物具有强力吸附作用，通过静电力作用达到杀灭或抑制病原微生物，不会产生耐药性[9-12]。经国家食品药品监督管理局 (SFDA) 批准为Ⅲ类医疗器械。适用于因病原微生物引起的炎症感染创面及物理、机械、热力因素引起的创面，以杀灭和隔离细菌、真菌及病毒。

本研究显示，我院内分泌科及骨科 2008 年 8 月至 2013 年 7 月收治的 168 例糖尿病足感染患者分泌物细菌培养结果显示分离率由高到低分别为：金黄色葡萄球菌、铜绿假单胞菌、产气肠杆菌、阴沟肠杆菌、不动杆菌、表皮葡萄球菌。由于不同病原微生物对各种抗菌药物表现出不同程度的耐药性，耐药性成为抗菌药物治疗糖尿病足感染的一大难题。

通过试验验证，糖尿病足主要的致病菌随着抗菌药物的使用，敏感性也在不同程度的降低，有的甚至耐药率为 100%。但这 6 种细菌对 JUC 长效抗菌材料耐药率仅为 0。

物理抗微生物膜作为一种创新物理方法抗菌的专利技术，不同于传统抗菌药物的化学或生物学方法，而是采用物理学方法抗菌，可避免抗菌药物导致的耐药菌产生，为临床治疗糖尿病足提供了新的途径和方法。

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表 2　主要病原菌对常用抗菌药物与 JUC 长效抗菌材料的耐药率（%）

抗菌药物	金黄色葡萄球菌	铜绿假单胞菌	产气肠杆菌	阴沟肠杆菌	不动杆菌	表皮葡萄球菌
青霉素	96.5	–	–	–	–	83.8
左氧沙星	47.6	32.2	22.1	40.2	21.6	30.2
氨苄西林	90.6	99.8	70.5	94.6	55.9	48.6
苯唑西林	100.0	70.5	94.6		0.0	
哌拉西林	46.5	35.2	29.2	30.5	66.2	37.6
庆大霉素	65.8	53.6	7.5	28.1	47.9	25.12
头孢唑林	23.5	97.8	75.3	89.3	94.6	70.21
头孢他啶	72.5	23.5	30.6	62.3	52.7	5.6
JUC	0.0	0.0	0.0	0.0	0.0	0.0