Sterilizasyonda ve Dezenfeksiyonda Yeni Ne Var?

Yeni Antiseptikler
Antiseptik Direnç Sorunu

Prof Dr Nefise Öztoprak Çuvalcı

SBÜ Antalya Eğitim ve Araştırma Hastanesi

Enfeksiyon Hastalıkları ve Klinik Mikrobiyoloji Kliniği

Öğrenim Hedefleri

- **Yeni çıkan antiseptikler**
- **Antiseptiklerdeki direnç sorunu**

Antiseptikler - Tarihçe

- Yara bakımı antik Mısır'a kadar uzanır
- **Yara bakımı/ Antiseptik bilgisi:** Oymalardan, antik papirüslerden, Sanskritçe belgelerden, dini metinlerden, bilimsel çalışmalardan ve edebiyattan elde edilir
- Mezopotamya kil tabletlerinde (yaklaşık MÖ 2500) geçen en eski kanıt;

  Yara bakımı:

  1. **yarayı yıkama**
  2. **topikal tedaviler (sıvalar)**
  3. **bandajlama**

- Yarayı Sümerler **birayla;** Yunanlılar **kaynamış su, sirke veya şarapla** yıkamış
- Bitkilerden, hayvansal ürünlerden ve minerallerden (kil ve metaller) topikal ilaçlar hazırlamış
- **Bandaj** için **yapraklar, otlar, yün veya keten** kullanmış

Antiseptikler Tarihçe

3 Broughton G, Janis JE, Attinger CE. A brief history of wound care. *Plast Reconstr Surg* 2006; **117** Suppl 7: 6S–11S.

4 Forrest RD. Development of wound therapy from Dark Ages to the present. *J R Soc Med* 1982; **75**: 268–73.

5 Hugo WB. A brief history of heat and chemical preservation and disinfection. *J Appl Bacteriol* 1991; **71**: 9–18.

- 19.yy itibaren kimyasal endüstrinin gelişmesi, enfeksiyonu tedavi etmede ve önlemede kullanılan antimikrobiyal ajanlar sağlamaya başladı
- 1820'lerde **klor solüsyonları** hastane yüzeylerini temizlemek için kullanıldı

  sonra **klorlu kireç** doğum uzmanlarının ellerini dezenfekte etmek için kullanıldı

- 1818'de **Hidrojen peroksit** keşfedildi, ancak antiseptik olarak 19. yy sonlarına kadar kullanılmadı
- 1825'te **Sodyum hipoklorit** Labarraque tarafından ilk olarak yaralara uygulanmış
- 1915'te **EUSOL (hipokloröz asit) ve Dakin solüsyonu (borik asitli sodyum hipoklorit)** formüle edildi

Antiseptikler Tarihçe

JAC Antimicrob Resist
doi:10.1093/jacamr/dlab027

JAC-Antimicrobial Resistance

Antimicrobial stewardship of antiseptics that are pertinent to wounds: the need for a united approach

Jean-Yves Maillard [1]*, Günter Kampf[2] and Rose Cooper[3]

- 20.yy ikinci yarısından itibaren daha iyi tolere edilen iyileştirilmiş antiseptik solüsyonlar klinik uygulamaya girdi

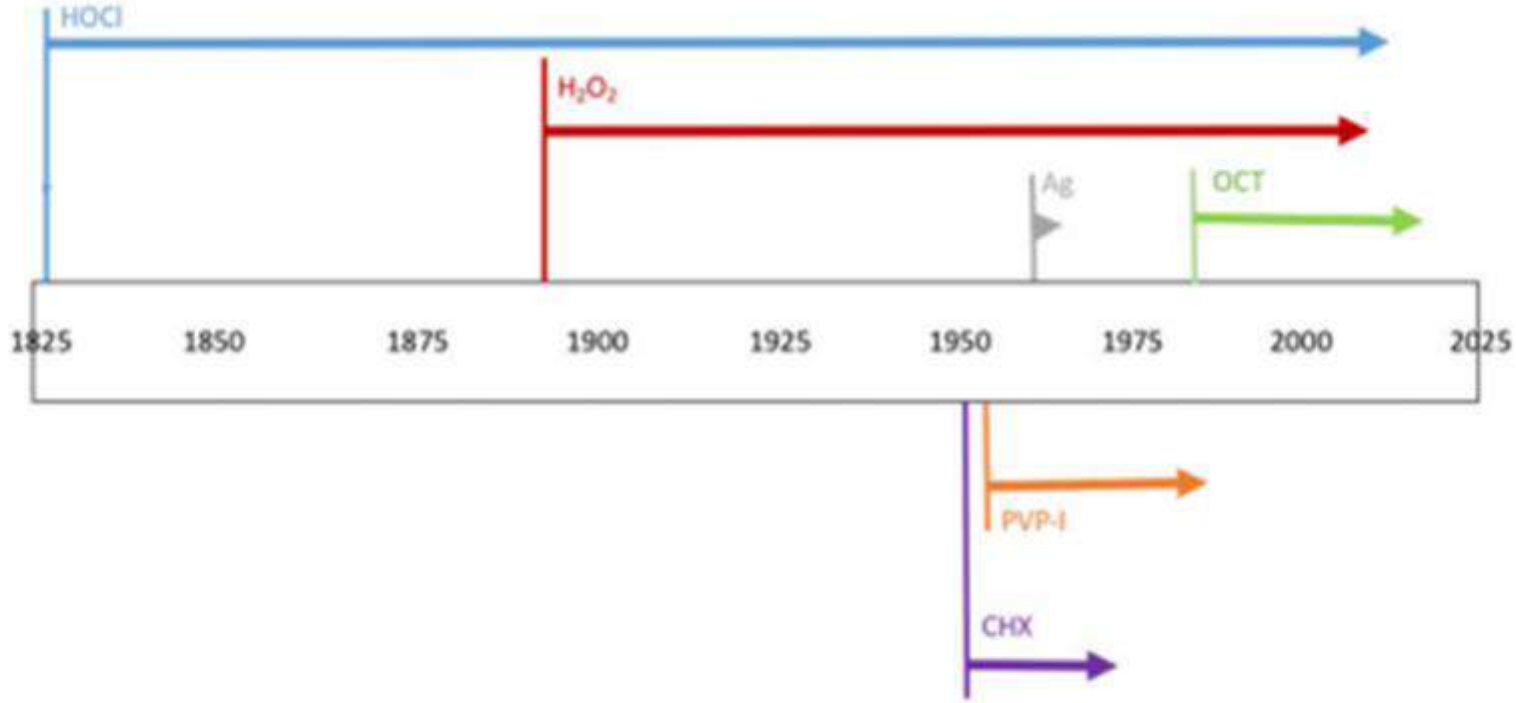


Figure 1. Biocide deployment and time for decreases in susceptibility to be documented. Each arrow's length represents the time between clinical use and reported bacterial non-susceptibility.

Antiseptikler

JAC Antimicrob Resist
doi:10.1093/jacamr/dlab027

2021

JAC-Antimicrobial Resistance

Antimicrobial stewardship of antiseptics that are pertinent to wounds: the need for a united approach

Jean-Yves Maillard [1]*, Günter Kampf [2] and Rose Cooper [3]

Table 1. Events that have influenced the development of modern antimicrobial wound care

Intervention	Date of introduction	Location	Use
Wine, vinegar, beer	antiquity	Mesopotamia, Egypt, Greece	wound cleansing
Honey	antiquity	Mesopotamia, Egypt, Greece, India, China	in ointments applied to various wounds
Metallic silver	circa 420 BCE	Persia	storage of potable water
Mercuric chloride	Middle Ages	France and Arabic civilizations	various wounds
Silver nitrate	eighteenth century	Europe	treatment of ulcers
Iodine	1829	France	various wounds
Chlorinated water and chlorinated lime	1820s 1847	UK Austria	hospital cleaning antiseptic handwashing
Sodium hypochlorite	1825	France	various wounds
Creosote (wood)	1837	Ireland	dressing venereal ulcers, fistula and nasal septum
Phenol	1860	Germany	wound antiseptic
Carbolic acid	1865	UK	treatment of compound fractures
Sterile cotton/gauze	1891	USA	wound dressing
Hydrogen peroxide	1887	UK	wound antiseptic
Silver foil	1895	USA	surgical wound dressing (hernia)
Tulle gras (gauze with soft paraffin, balsam of Peru and olive oil)	1915	France	non-adherent wound dressing
EUSOL	1915	UK	wound antiseptic
Dakin's solution	1915	UK	wound antiseptic
Chlorhexidine digluconate	1954	UK	antiseptic hand scrub and irrigating wounds
Povidone iodine	1956	USA	wound antiseptic
Cadexomer iodine	1980s	Sweden	wound dressing
Silver nitrate	1964	UK	over-granulating wounds
Silver sulfadiazine	1968	USA	infection control in burns
Polihexanide	1991	Switzerland	antiseptic solution
Octenidine dihydrochloride	1988	Germany	antiseptic solution
Medical honey	1999	Australia	topical treatment of wounds
Reactive oxygen species	2006	Belgium and UK	enzyme alginogels[a]

Here, the term antiseptic refers to a non-antibiotic antimicrobial (see section 3).
[a]Note that alginogels are gels rather than dressings.

Etkin Bir Antiseptikte Bulunması Gereken Temel Özellikler

- **Geniş spektrumlu olmalı**
- **Hızlı ve kalıcı etkili olmalı**
- **Kullanımı kolay olmalı**
- **Kötü kokulu olmamalı**
- **Ciltte ve mukozada tahriş edici, doku hasarı etkisi olmamalı**
- **Toksik, karsinojen, allerjen olmamalı**
- **Raf ömrü uzun ve bu sürede etkin olmalı**
- **Direnç hiç olmamalı veya düşük olmalı**

Yeni (!) Antiseptikler

1. **Hipokloröz asit**
2. **Oktenidin Dihidroklorür**
3. **Poliheksanid (Polihexanide Biguanide)**
4. **Nanoteknolojik Antisepitkler**
5. **İyot Kompleksleri (Yavaş salınımlı)**
6. **Esensiyal Yağ Türevleri (Timol, Karvakrol, Eugenol vb)**

Review

Wound Antiseptics and European Guidelines for Antiseptic Application in Wound Treatment

Pharmaceuticals **2021**, *14*, 1253

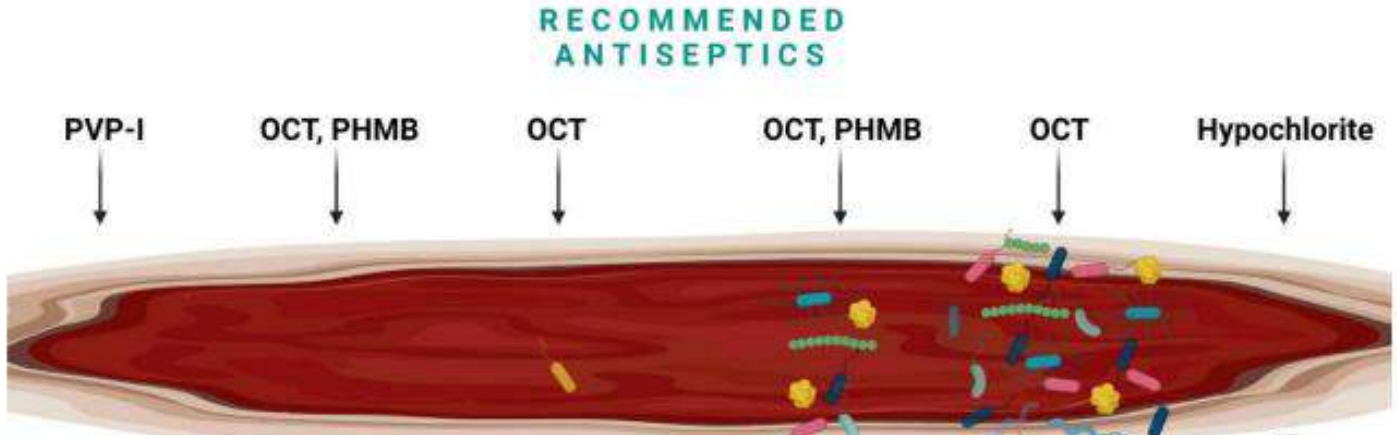


Table 2. Summary of first and second choice measures for the treatment of specific wounds [28–30].

Indication	Anti-Bacterial Substance	
	First Choice	Second Choice
Wounds without drainage	Hypochlorite	-
Critically colonized wounds, wounds at risk of infection	PHMB (0.02%, 0.04%, 0.1%), OCT 0.05%	OCT/hypochlorite, silver
Bitten, stab and gunshot wounds	PVP-I	Hypochlorite
Wounds colonized or infected by MDRO	OCT	OCT 0.05%, PHMB, silver
Decontamination of acute and chronic wounds	PHMB, hypochlorite	-
Burns	PHMB, OCT 0.05%	OCT/hypochlorite
Rinsing the peritoneal cavity	Hypochlorite	-
Risk of PNS exposure	Hypochlorite	PVP-I
SSI prophylaxis	OCT	-

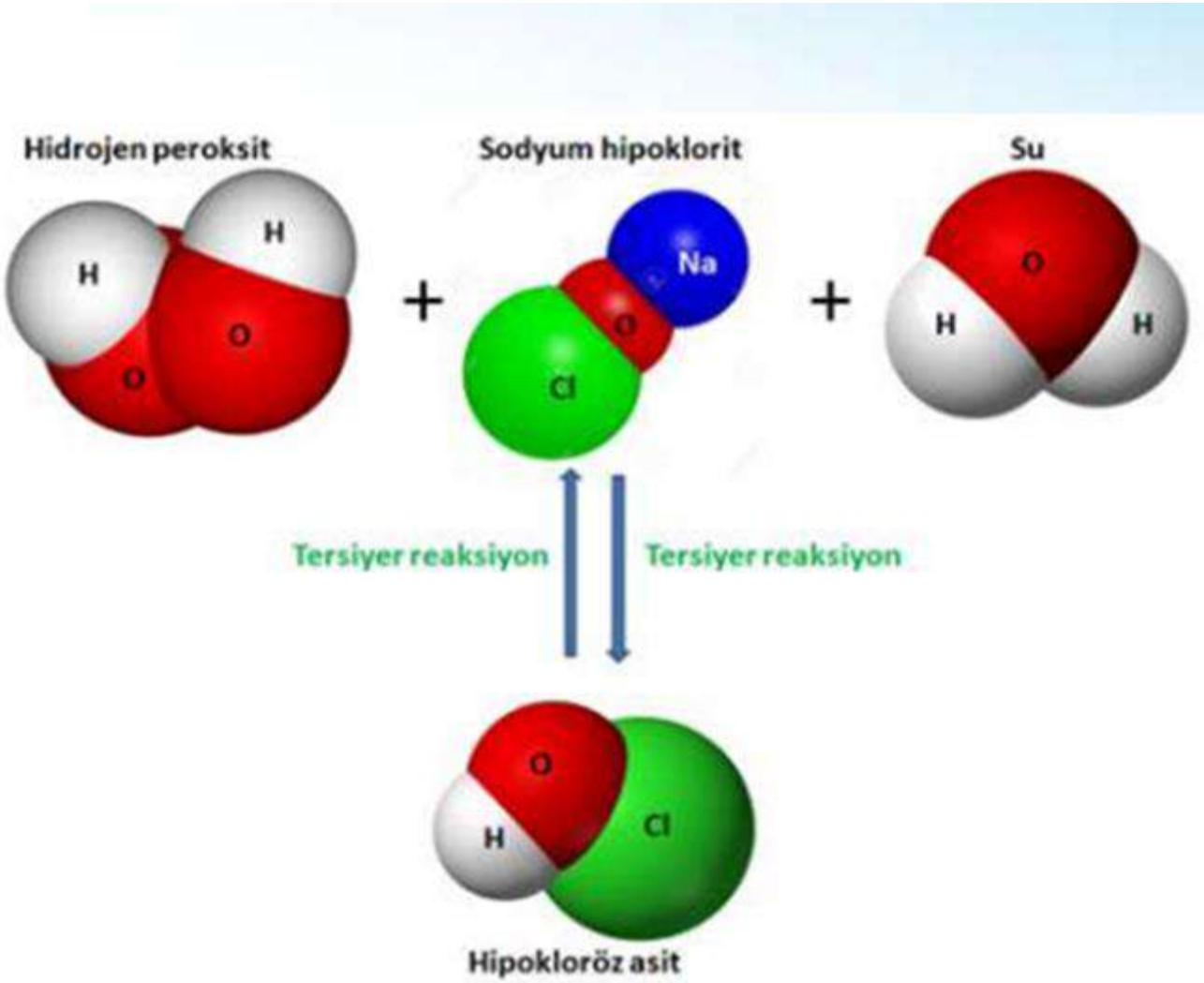
Hipokloröz Asit- Süperokside Su

İthal Ürün !!

Fiyatı daha yüksek

DMO’da 100 ml’lik formu var !!

Hipokloröz Asit (HOCl)



.914 ilk kullanım (I. Dünya Savaşı)

ek için üretilen **doğal bir madde**

de **çok güçlü oksidan etkisi** var

lar

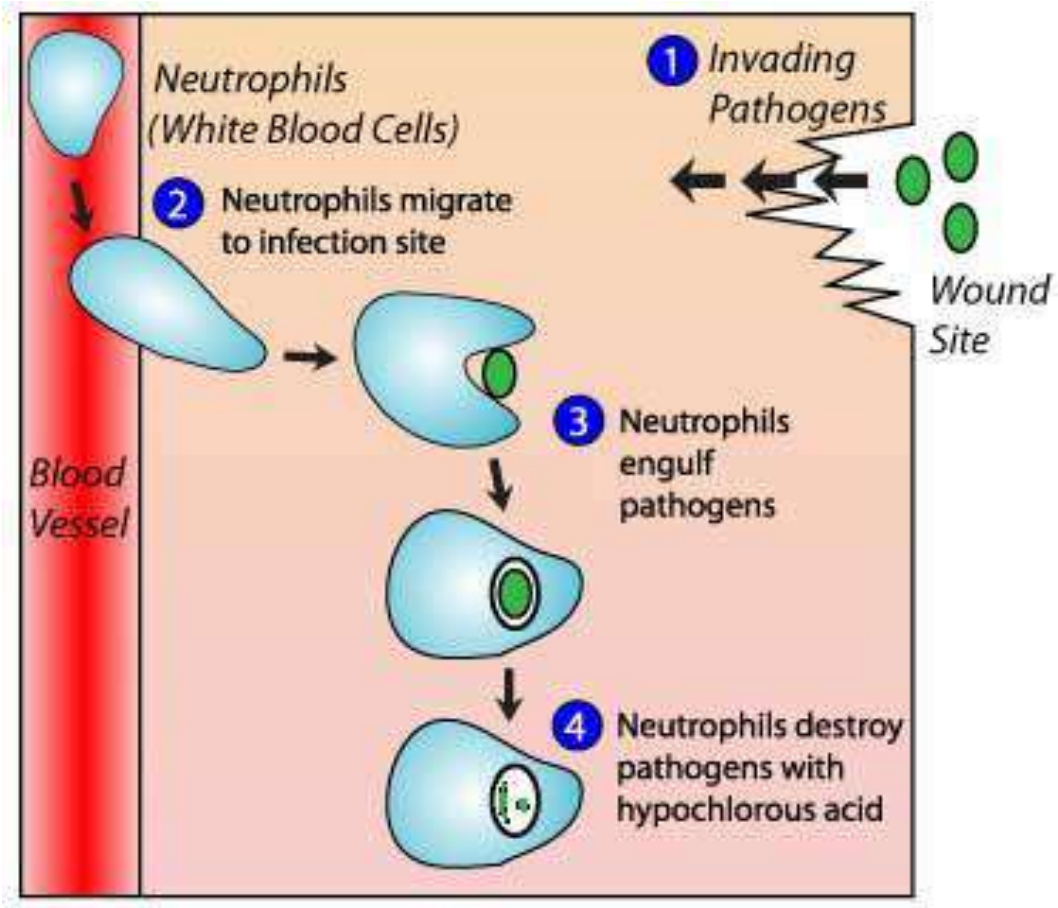
(NaCl) elde edilir

tan değildir, toksik etkisi yok

ler, zarflı virüsler, mantarlar, sporlar

rahi yıkama, ….

HİPOKLORÖZ ASİT VÜCUDUMUZDA NASIL OLUŞUR VE ÇALIŞIR?



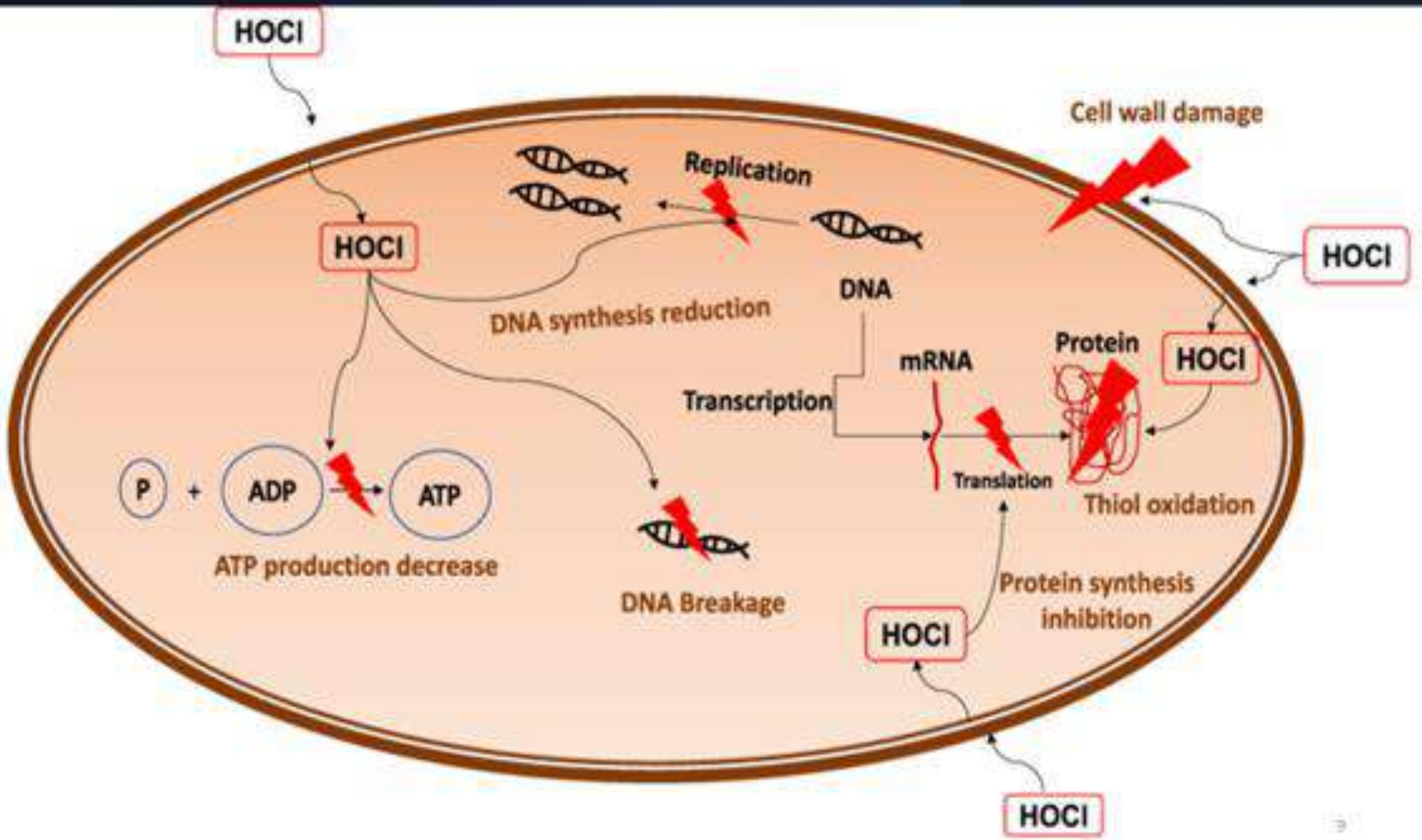
Hipokloröz asit, bilinen en doğal ve en güçlü antimikrobiyal molekül olarak tanımlanır

Tüm bakterileri, sporları, mantarları, virüsleri, hatta zorlu Clostridium difficile'yi bile saniyeler içinde yok eder

Çamaşır suyuna göre 70 ila 100 kat daha iyi dezenfekte eder ve %100 güvenlidir

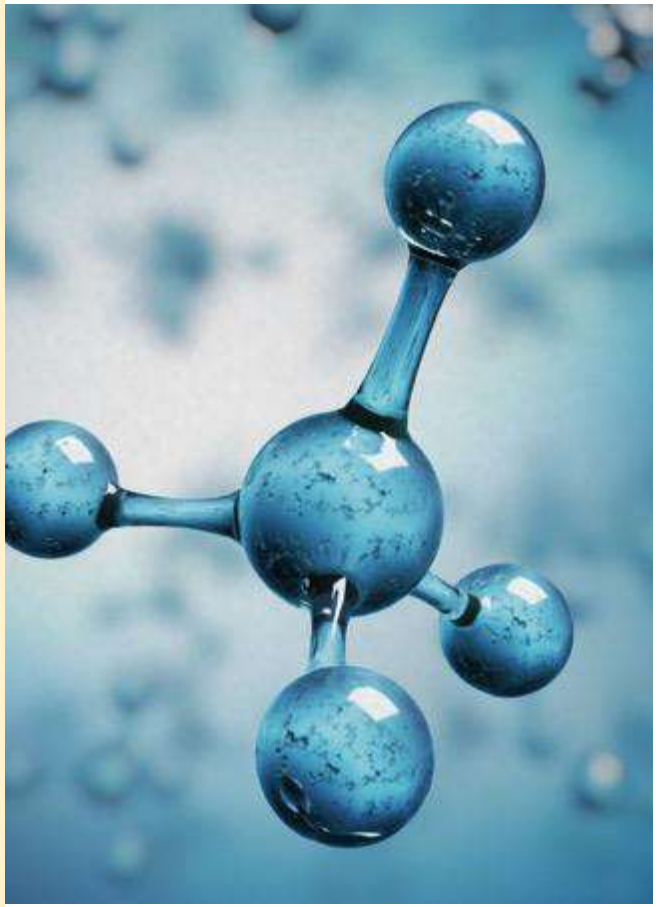
Hipokloröz' ün

Mikroorganizmalar üzerindeki çoklu etki mekanizması



ÇOK GÜÇLÜ ETKİ MEKANİZMASI

- TEMAS YOLUYLA ÇALIŞIR
- UYGULANDIĞI ALANDA MİKROORGANİZMA İLE TEMAS ETMESİ YETERLİ !
- ETKİ BAŞLANGICI ÇOK HIZLIDIR
  - «0» saniyede başlar
- TEMAS EDER ETMEZ
- BAKTERİ VE MANTARLARIN HÜCRE DUVARLARINDAN SODYUM VE ELEKTRON BAĞLAYARAK
  - Hücre duvarı bütünlüğünü bozar, geçirgenliği artırır,
  - Ozmotik basıncı değiştirir,
  - Ozmotik şok ile saniyeler içinde parçalanmalarını sağlar

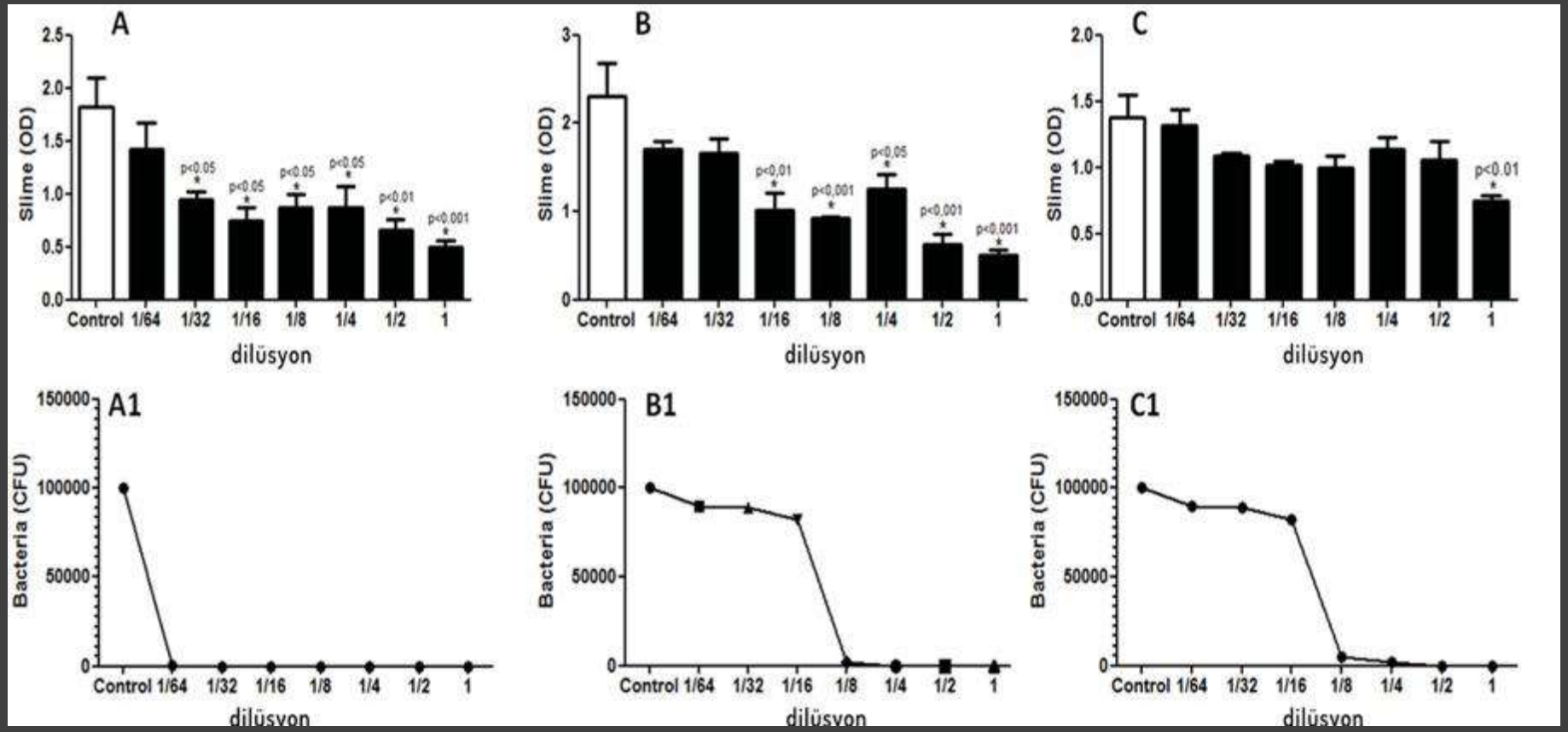


MANTARLAR

- Acremonyum kliense
- Aspergillus flavus
- Fusarium solani
- Mucor indicus
- Aspergillus Fumigatus
- Aspergillus Niger
- Candida Albicans
- Candida parapsilosis
- Epidermophyton Floccosum*
- Microsporum
- Rhizopus Oryzae
- Trichophyton Rubrum*
- Trichophyton Tonsurans*
- Trichophyton Verrucosum*

ır
motropica
ruginosa **
itidis
yphi A
ens
ureus (Mrsa/mssa)
pidermidis
aemolyticus
lominis
aprophyticus
as Maltophilia
eumoniae
ogenes
halis
ori

VİRÜSLER
Adenoviridae'lar: Adenovirus
Flaviviridae: Hepatit C Virus
Herpersviridae: Ebstein-Barr Virus, Herpes Simplex Tip 1,2,8 Cytomegalovirus - Varicella Zoster
Hepadnaviridae: Hepatitis B Virus
Hepatitis A Virus
PARAZİTLER
ACANTHAMOEBA SPP.
TRICHOMONAS VAGİNALİS
Poliovirus
Reoviridae: Rota Virus
Respiratory Syncytial Virus (Hrsv)
Retroviridae: HIV
Rhabdoviridae: Rabies Virus
Togoviridae: Rubella Virus

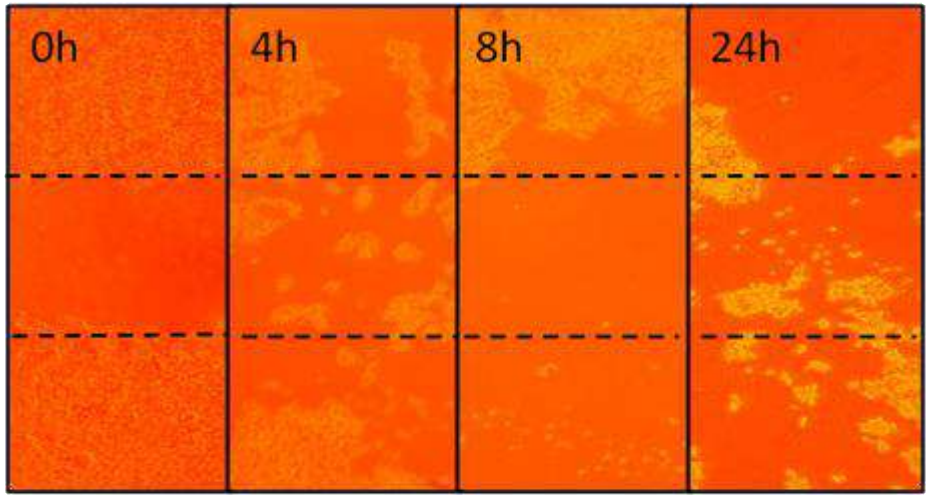


A: *S. Aureus* **B: *P. Aeruginosa*** **C: *C. Albicans***

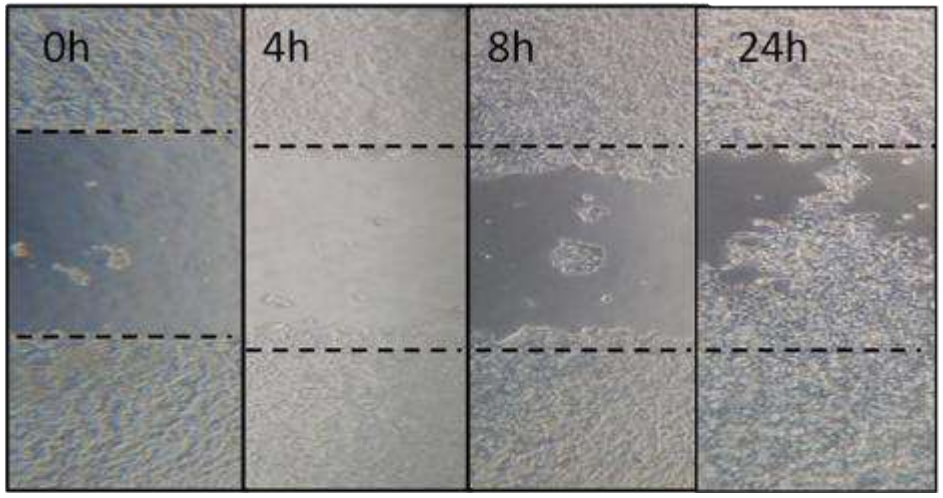
Biyofilm ve Biyofilm Altındaki Mikroorganizma Üzerine Etkinlik

HİPOKLORÖZ ASİT & POVİDON İODİN FİBROBLAST'LAR ÜZERİNE ETKİLERİ

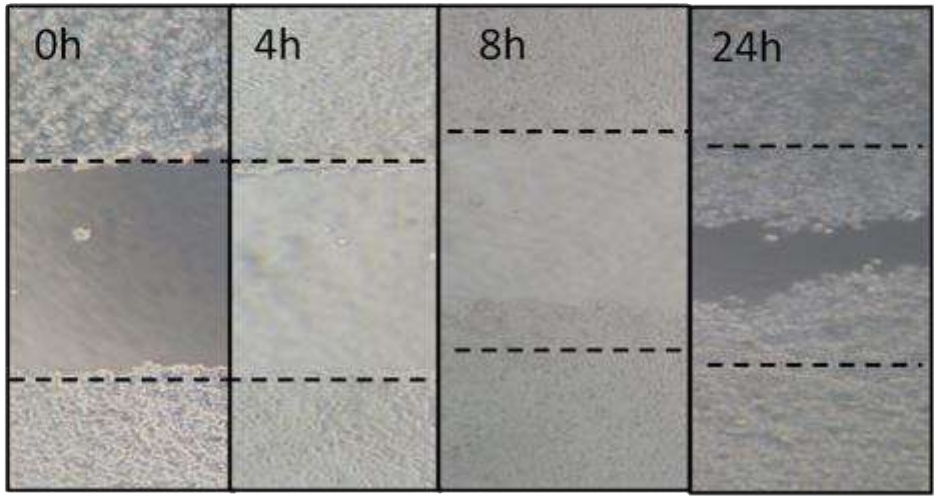
S.SAKARYA-B.ERTUĞRUL 2013 ADÜ ENF.HAST.KLİNİĞİ



Povidone iodine



HOCl



control

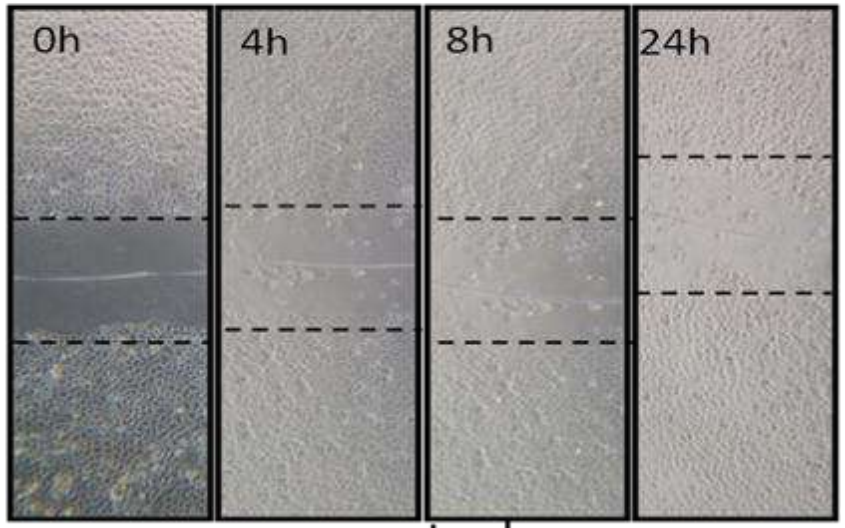
HİPOKLORÖZ ASİT & POVİDON İODİNE KERATİNOSİTLER ÜZERİNE ETKİLERİ

S.SAKARYA-B.ERTUĞRUL 2013 ADÜ ENF.HAST.KLİNİĞİ

FİBROBLAST VE KERATİNOSİTLERİN HASARLI DOKUYA PROLİFERASYONUNU (GÖÇÜNÜ) ARTIRARAK İYİLEŞMEYİ HIZLANDIRIR

Povidone iodine

HOCl



Klinik Kullanımları

Evaluation of hypo washes in the trea chronic venous leg

• **Objective:** Hypochlorous acid (HOCl) is a highly mic fungi. Using quantitative microbiology, preliminary studie the bacterial burden in chronic venous leg ulcers. The st additional treatment for chronic venous ulcers that have

• **Method:** On the basis of previous reports we design controls, in that only patients who failed to achieve a 4 treatment (compression bandaging) received HOCl wa

• **Results:** Of 30 patients admitted to the study, 10 ac standard treatment. In addition to the standard compre given HOCl washes over 12 weeks. Of the 20 ulcers, ni over 60%. All patients became free of pain.

• **Conclusion:** These findings confirm the clinical effic hypochlorous washes. Use of HOCl washes as an adjun appreciably increases healing and rapidly relieves pain.

WOUNDS 2014;26(12):342-350

From the [1]Adnan Menderes University, School of Medicine, Department of Infectious Diseases and Clinical Microbiology, Aydin, Turkey; [2]Adnan Menderes University, Adubiltem Research and Development Center, Aydin, Turkey; [3]Ataturk University, School of Medicine, Erzurum, Turkey

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Disclosure: The authors disclose no financial or other conflicts of interest.

Hypochlorous Acid: An Ideal Wound Care Agent With Powerful Microbicidal, Antibiofilm, and Wound Healing Potency

Serhan Sakarya, MD[1]; Necati Gunay, MS[2]; Meltem Karakulak, MS[3]; Barcin Ozturk, MD[1]; Bulent Ertugrul, MD[1]

Abstract: *Introduction.* Chronic wounds and the infections associated with them are responsible for a considerable escalation in morbidity and the cost of health care. Infection and cellular activation and the relation between cells are 2 critical factors in wound healing. Since chronic wounds offer ideal conditions for infection and biofilm production, good wound care strategies are critical for wound healing. Topical antiseptics in chronic wounds remain in widespread use today. These antiseptics are successful in microbial eradication, but their cytotoxicity is a controversial issue in wound healing. *Objective.* The aim of this study was to investigate the effect of stabilized hypochlorous acid solution (HOCl) on killing rate, biofilm formation, antimicrobial activity within biofilm against frequently isolated microorganisms and migration rate of wounded fibroblasts and keratinocytes. *Materials and Methods.* Minimal bactericidal concentration of stabilized HOCl solution for all standard microorganisms was 1/64 dilution and for clinical isolates it ranged from 1/32 to 1/64 dilutions. *Results.* All microorganisms were killed within 0 minutes and accurate killing time was 12 seconds. The effective dose for biofilm impairment for standard microorganisms and clinical isolates ranged from 1/32 to 1/16. Microbicidal effects within the biofilm and antibiofilm concentration was the same for each microorganism. *Conclusion.* The stabilized HOCl solution had dose-dependent favorable effects on fibroblast and keratinocyte migration compared to povidone iodine and media alone. These features lead to a stabilized HOCl solution as an ideal wound care agent.

Key words: hypochlorous acid, biofilm, wound healing, fibroblast, keratinocyte

Klinik Kullanımlar-YARA TEDAVİSİ

JIMSA October - December 2011 Vol. 24 No. 4

Recent Advances in Management of Chronic Non healing Diabetic Foot Ulcers

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MD, Foot Fellowship,Chicago, USA, Sr.Diabetic Foot Specialist & Stem Cells Therapist

Fortis C-DOC, Chirag Enclave, New Delhi, India

- Pansuman ve instalasyon VAC tedavisinde tek ajan olarak önerilmiştir.

KLİNİK KULLANIMLARI

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journal homepage: www.elsevier.com/locate/msec

Disinfection of titanium dioxide nanotubes using super-oxidized water decrease bacterial viability without disrupting osteoblast behavior

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Sterilization
Bacterial viability
Super-oxidized water

ABSTRACT

Amorphous titanium dioxide (TiO_2) nanotubes (NTs) on Ti6Al4V alloy were synthesized by anodization using a commercially available super-oxidized water (SOW). The NT surfaces were sterilized by ultraviolet (UV) irradiation and disinfected using SOW. The adhesion and cellular morphology of pig periosteal osteoblast (PPO) cells and the behavior of *Staphylococcus aureus* (*S. aureus*) cultured on the sterilized and disinfected surfaces were investigated. A non-anodized Ti6Al4V disc sterilized by UV irradiation (without SOW) was used as control. The results of this study reveal that the adhesion, morphology and filopodia development of PPO cells in NTs are dramatically improved, suggesting that SOW cleaning may not disrupt the benefits obtained by NTs. Significantly decreased bacterial viability in NTs after cleaning with SOW and comparing with non-cleaned NTs was seen. The results suggest that UV and SOW could be a recommendable method for implant sterilization and disinfection without altering osteoblast behavior while decreasing bacterial viability.

…e
…ARDA

…TEZİN
…LIR

Klinik Kullanımlar

Jpn J Thorac Cardiovasc Surg. 2003 Oct;51(10):511-4.

Management with closed irrigation for post-sternotomy mediastinitis: experience with the use of electrolyzed strong acid aqueous solution.

Ohuchi S[1], Kawazoe K, Ishihara K, Izumoto H, Eishi K.

Author information

1 Department of Cardiovascular Surgery, Iwate Medical University Memorial Heart Center, 1-2-1 Chuohdori, Morioka, Iwate 020-8505, Japan.

CONCLUSIONS:

Our experience of closed irrigation and drainage suggests that it can yield satisfactory results after post-sternotomy mediastinitis, comparable to other reported results with or without muscle flaps.

of therapy for mediastinitis.

Klinik Kullanımlar

- Periton içi uygulamalar da etkin dekontaminasyon
- Yan etki yok

Effect of Electrolyzed Strong Acid Water on Peritoneal Irrigation of Experimental Perforated Peritonitis

AKIO KUBOTA[1], KEISUKE NOSE[2], TAKEO YONEKURA[2], TAKUYA KOSUMI[2], KATSUJI YAMAUCHI[2], and HARUMASA OYANAGI[2]

[1]Department of Pediatric Surgery, Osaka Medical Center and Research Institute for Maternal and Child Health, 840 Murodo-cho, Izumi, Osaka 594-1101, Japan
[2]Division of Pediatric Surgery, Kinki University School of Medicine, Osakasayama, Osaka, Japan

Abstract

Purpose. Electrolyzed strong acid water (ESAW) is generated by the electrolysis of a weak sodium chloride solution. Although ESAW is known to have a strong bactericidal activity and to be harmless to the living body, its effectiveness and safety in the treatment of perforated peritonitis has not been well established.

Methods. Male Wistar rats were used for the study. Three hours after cecal ligation and puncture, the cecum was resected and the peritoneal cavity was irrigated with 50 ml of saline (Group S, n=12) or ESAW (Group E, n=14). The 5-day survival rate was compared between the two groups. In another pair of animals (n=10 each), bacteria in the ascitic fluid were counted at 6 and 18 h after irrigation.

Results. No adverse effects of ESAW were observed in the experimental group. The 5-day survival rate was 25% (3/12) and 85.7% (12/14) in Groups S and E, respectively ($P < 0.01$). The bacterial count at 18 h after the irrigation in Groups S and E was $(5.0 \pm 2.5) \times 10^5$/ml and $(2.2 \pm 2.0) \times 10^4$/ml, respectively ($P < 0.0001$).

Conclusion. Peritoneal lavage with ESAW had no adverse effect, and achieved more effective decontamination than saline for perforated peritonitis. Therefore, the results of this study are considered to warrant and support the clinical application of ESAW.

Introduction

Electrolyzed strong acid water (ESAW) is generated by the electrolysis of a weak sodium chloride solution (20 mM NaCl). Its physiological and chemical characteristics include a pH of 2.7, an oxidative-reduction potential of 1000–1100 mV, a dissolved oxygen concentration of 10–30 ppm, and a chlorine concentration of 30–40 ppm, or 1.2 mM as hypochlorous acid,[1,2] which has strong bactericidal activity[3–5] and disinfection potential against viruses.[6–8] The feasibility and safety of ESAW irrigation in wound infection or ocular surface disinfection have been confirmed in animal models.[9,10] However, few applications of body cavity lavage with ESAW in clinical cases have been reported in the literature.[11–14] In order to establish its safety and effectiveness for peritoneal irrigation in perforated peritonitis, an experimental study was conducted.

Materials and Methods

Subjects

Wistar male rats (Nihon Clea, Tokyo, Japan) 7 weeks of age, weighing about 250 g, which were raised prelimi-

Klinik Kullanımlar- Göz

- Göz içi protez uygulamalarında profil

Cornea. 2015 December ; 34(12): 1599–1605. doi:

Fungal Infections Following Bos Implantation: Literature Review of Hypochlorous Acid

Silvia Odorcic, MD, FRCSC, Wolfgang Haas, Dohlman, MD, PhD

Conclusions—Fungal infections remain a lifel implantation. There is a growing need for a stand the developing world. The rapid broad-spectrum hypochlorous acid against all fungi tested makes prophylaxis in KPro patients.

Journal of Environmental Protection and Ecology 19, No 3, 1397–1404 (2018)

Public health – environmental medicine

STABILISED HYPOCHLOROUS ACID: A NEW THERAPEUTIC STRATEGY AGAINST DANGEROUS PARASITIC EYE INFECTION AGENT *Acanthamoeba* spp.

I. YILDIZ[a]*, O. YILMAZ[b], E. TILEKLIOGLU[a], S. SAKARYA[c], H. ERTABAKLAR[a]

Abstract. *Acanthamoeba* species are protozoan parasites that cause serious diseases in human. It is significant to investigate new treatment agents to combat the parasite which is very difficult to treat. The recent studies about stabilised hypochlorous acid indicated that with a rapid killing effect on different types of microorganisms, it could be used as a treatment agent for *Acanthamoeba* infections. Thus, we aimed to investigate the effect of stabilised hypochlorous acid on *Acanthamoeba*. Stabilised hypochlorous acid at serial dilutions of 1/2, 1/4, 1/8, 1/16, 1/32, and 1/64 was used in different time course. The direct microscopy for time-kill assay and Trypan blue assay were used to determine the effective dilutions and time exposure of stabilised hypochlorous acid to live form of parasite. We determined that the effect of stabilised hypochlorous acid was reached at 96 and 84% (dilution of 1/2 and 1/4, respectively) at the end of 90 min. The effect of stabilised hypochlorous acid was dose- and time-dependent. Stabilised hypochlorous acid solution could be used for eye infections due to the its safety feature. Since its effective feature at 1/2 and 1/4 dilutions within 0–10 min, it could be a new treatment agent to combat the parasite and its infections.

Keywords: stabilised hypochlorous acid, *Acanthamoeba*, eye infections, biofilm.

AIMS AND BACKGROUND

pH 7.1, Oxidation reduction potential (ORP) 871 MV and its stability were 24 months (NPS Biosidal, Istanbul, Turkey).

Klinik Kullanımlar

- Nazal irrigasyon sonu
  - % 99 bakterisidal (MRSA
    pnomoniae, H.influenzae)
    Aspergillus fumigatus)
  - İnfluenza A virüste 3.2 l
  - Nazal epitel sitotoksisite

The Laryngoscope
Lippincott Williams & Wilkins

Effects of a Low Cor Hypochlorous Acid I on Bacteria, Fungi,

Hyun Jik Kim, MD; Jeung-Gweon Lee, MD; Ju
Hyung Kwon Byeon, MD; Joo-Heon Yoon, MD

Objectives/Hypothesis: Saline irrigation would
more effective for chronic sinusitis patients if it had ba
tericidal effects. Low concentrations of hypochlorous ac
may be used as a nasal irrigation solution. First,
developed a 0.85% NaCl solution by adding NaCl to t
water (pH 7.0 and 8.4) and measuring the concentrati
of free chlorine and hypochlorous acid after giving t
solution a short electrical impulse of 20 seconds. Then

Periodontal hastalıkların tedavisi

Yapılan çalışmalarda, yumuşak doku ve kemik dokuda;

- İnflamasyonu azaltıp
- Yara iyileşmesini hızlandırdığı

The role of hypochlorous acid as one of the reactive oxygen species in periodontal disease

*Chong-Hou Sam,[1] Hsein-Kun Lu[2]**

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KEY WORDS:
hypochlorous acid;
NF-κB;
periodontitis;
taurine chloramine;
transcription factor AP-1

Hypochlorous acid (HOCl) has both proinflammatory and anti-inflammatory properties, and seems to play an important role in the immune system. The regulation of normal flora contributes to periodontal health, and HOCl seems to have the ability to attack Gram-negative pathogens during periodontitis. Furthermore, high concentrations of HOCl promote healing by regulating cytokines and growth factors, killing pathogens through chlorination or oxidation, and modulating inflammation through the effects on nuclear factor κB and activator protein-1 of monocytes. After chlorination of taurine by HOCl, taurine chloramine is mostly an anti-inflammatory agent and enhances healing. Neither HOCl nor taurine chloramine are common in clinical applications owing to a lack of studies in animal and human models. Both compounds may be suitable as periodontal medication, as they are good antimicrobial agents, inflammation modulators, and healing promoters.

Sam CH, J.Dental Science. 2009;4:45-54.

Oktenidin Dihidroklorür (Octenidine Dihydrochloride)

- Sentetik katyonik bir antiseptik
- 1980'lerde Almanya'da geliştirildi son yıllarda kullanımı yaygınlaştı
- **Spektrum:** Gram pozitif ve Gram negatif bakteriler, mantarlar (Candida türleri dahil), Zarflı virüsler (HIV, HBV, HCV vb), MRSA ve VRE gibi dirençli suşlara da etkili
- **Kullanım:** Preop cilt antisepsisi, Yara temizliği ve bakımı, kateter giriş yeri antisepsisi, mukozal antisepsi (ağız, vajen vb)
- **Avantaj:** Uzun süreli antimikrobiyal etki gösterir (**rezidüel etkisi var**) Klorheksidine göre daha az toksik ve daha az direnç oluşturuyor, renk bırakmaz, lekelemez

Oktenidin Dihidroklorür

- **Direnç gelişim potansiyeli çok düşük**
- **Gebelerde ve yenidoğan bebeklerde** kullanılabilir
- Yara bakımında cilt esnekliğini bozmaz, **daha az skar ve keloid** oluşturur
- **Kısa temas süresinde (1 dk) ve çok düşük konsantrasyonlarda etkili**
- **Anti-inflamutvar ve immünmodülatör etkisi var**
- Dokuya basınçla (enjektörle vb) uygulanırsa **doku hasarı** oluşturabilir !!
- Doğrudan **kulak zarında, periton veya mesanede kullanılmamalı** !!

Oktenidin Dihidroklorür (Octenidine Dihydrochloride)

Poliheksanid (Polihexanide Biguanide-PHMB)

Poliheksametilen Biguanid

- Yapısal olarak yaradaki keratinositler ve nötrofiller tarafından üretilen antimikrobiyal peptidlere benzer yapıdadır
- Bakterisidal etki için uzun süreli temas gerektirir (15 dk)
- **Antibakteriyel direnç bildirilmemiş**
- Güvenlidir, iyi tolere edilir
- **Doku hasarı yapmaz,** gözde, burunda kullanılabilir

Nanoteknolojik Antiseptikler

- **Gümüş nanopartiküller (AgNPs), çinko oksit nanopartikülleri (ZnONPs), bakır nanopartikülleri (CuNPs)** gibi bileşiklerle geliştirilmiştir
- **Spektrum:** Gram pozitif (MRSA dahil) ve negatif bakteriler, mantarlar, zarflı ve zarfsız virüsler,
- **Kullanım:** Diş macunu, deodorant vb ürünlerde, özellikle yanık tedavisinde kullanılan yara örtüleri, kateter ve tıbbi implantlarda ve nanogümüş kaplı gazlı bezlerde kullanılır
- **Avantaj:** Uzun süreli yavaş salınımlı antimikrobiyal etki, daha az miktarda aktif madde ile hedefe yönelik etki, biyofilme etkili, düşük toksisite ve direnç gelişimini azaltma potansiyeli
- **Uyarı:** Gümüş NP argyria (deri ve mukozada mavimsi gri renklenme) yapabilir, nadiren kalıcıdır !

İyot Kompleksleri

- En yaygın formu Povidon iyot (iyodun polivinilpirolidon ile kompleks formu)
- Son yıllarda geliştirilen **nanoformülasyonlar ve yavaş salınımlı iyot taşıyıcı sistemler (iyot- jel, film kaplama)** klasik formdan daha etkili ve az yan etki mg

- **Spektrum:** Gram pozitif ve negatif bakteriler, zarflı ve zarfsız virüsler, mantarlar, protozoalar, sporlar
- **Kullanım:** Preop antisepsi, yara bakımı, mukozal antisepsi (vajinal iyot jeller), gargara ve burun spreyi
- **Avantaj:** Direnç gelişimi çok düşük, etki süresi yavaş salınımlı formlar ile daha uzun, antibiyotik kombinasyonu ile sinerjik etki
- **Uyarı:** Uzun süreli kullanımda tiroid fonksiyonlarının etkiler, hamilelerde dikkat!

Esansiyel Yağ Türevleri (Doğal Antiseptikler)

- Bitkilerden elde edilen uçucu yağların içerdiği fenolik bileşikler sayesinde antimikrobiyal etki oluşur
- **En Sık Kullanılanlar:**
  - **Timol (kekik yağı)**
  - **Karvakol (kekik ve mercanköşk)**
  - **Eugenol (karanfil yağı)**
  - **Terpinen-4-ol (çay ağacı yağı)**
  - **Mentol (nane)**
- **Spektrum:** Özellikle oral patojenlerde ağız hijyeninde çok etkili, Gram pozitif, Gram negatif bakteriler, mantarlar ve bazı zarflı virüsler

Esansiyel Yağ Türevleri

- **Kullanım:** ağız gargaraları, doğal el dezenfektanları ve sabunlar, cilt antisepsisi (özellikle çay ağacı yağı)
- **Avantaj:**
  - doğal kaynaklı
  - direnç gelişimi yok
  - sentetik antiseptiklere karşı allerjisi olanlar için alternatif,
  - anti-inflamatuvar ve analjezik etki sağlar (eugenol)
- **Uyarı:** Özellikle seyreltilmeden kullanıldığında deri tahrişi ve alerjik reaksiyonlar yapabilir

Antiseptikler ve Direnç

- Antiseptiklerde direnç gelişimi antibiyotik direncine göre daha az
- **Bir antiseptik sidal bir konsantrasyonda veya uygunsuz bir süre kullanıldığında direnç ortaya çıkabilir**

- Antibiyotik direncine yol açan mekanizmaların çoğu, antiseptik direnç mekanizmalarıyla benzer (eflüks pompalarının aşırı üretimi vb)
- QAC'ye özgü eflüks pompaları küçük çoklu ilaç direnci (SMR) ailesinin üyeleridir

Kwaśniewska, D.; Chen, Y.-L.; Wieczorek, D. Biological activity of quaternary ammonium salts and their derivatives. *Pathogens* **2020**, *12*, 459. [CrossRef]
Milani, E.S.; Hasani, A.; Varschochi, M.; Sadeghi, J.; Memar, M.Y. Biocide resistance in *Acinetobacter baumannii*: Appraising the mechanisms. *J. Hosp. Infect.* **2021**, *117*, 135–146. [CrossRef]
Coyne, S.; Courvalin, P.; Perichon, B. Efflux-mediated antibiotic resistance in *Acinetobacter* spp. *Antimicrob. Agents Chemother.* **2011**, *55*, 947–953. [CrossRef]

Antiseptik Direnci- Antimikrobiyal Direnç

- Biyositler, bakteri hücrelerindeki çok sayıda hedefle (16 adet) etkileşime girer
- Bakterisidal veya bakteriyostatik etki: etkilenen hedef sayısı ve hasarın şiddeti ile oluşur
- **Biyositler antimikrobiyal direnç genlerinin transferini de teşvik edebilir !!**

  - Yatay gen transferi *E. coli*'de klorheksidin diglukonat ile indüklenebilir
  - Antibiyotik direnç genlerinin ifadesi vanA *E. faecium*'da klorheksidin

klorheksidin diglukonat, oktenidin dihidroklorür ve povidon iyotun alkolle kombinasyonu daha uygun !!

Kampf, G. (2024). Antiseptic Stewardship for Skin Antiseptics. In: Antiseptic Stewardship. Springer, Cham. https://doi.org/10.1007/978-3-031-66074-0_20

Article

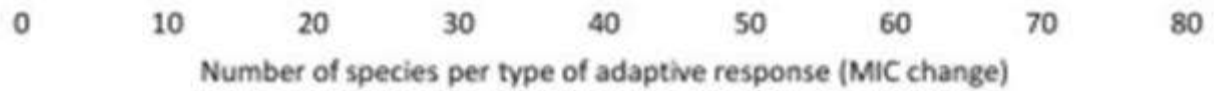
Evaluating the Effectiveness of Hospital Antiseptics on Multidrug-Resistant *Acinetobacter baumannii*: Understanding the Relationship between Microbicide and Antibiotic Resistance

Antibiotics **2022**, *11*, 614. https://doi.org/10.3390/antibiotics11050614

- **Mikrobisidal direnç biyofilmle direk ilişkili !!**
- **Duyarlı suşların da mikrobiyosidal direnç genleri içermesi dikkat çekici!!**
- **Bazı hastanelerde yalnızca patojen MDR ise izolasyon önlemleri uygulanıyor**
- PS suşları arasında bile mikrobisidal direnç bulgularımız göz önüne alındığında, hastaneler **duyarlı *A. baumannii* enfeksiyonlarında bile daha sıkı temas önlemleri dikkate almak isteyebilir!!**
- Hayatta kalan %0,1'lik alt popülasyon az sayıda bakteriyi temsil etse de, yine de **hastane salgınlarına** katkıda bulunabileceği akılda tutulmalı !!

and *qacA*. MDR strains did not survive more than PS strains in the presence of microbicides, but microbicide-resistant strains had higher survival rates under some conditions. Interestingly, the PS strains were more likely to possess microbicide-resistance genes. Microbicide resistance remains an important topic in healthcare and may be independent of antimicrobial resistance. Hospitals should consider stricter isolation precautions that take pan-susceptible strains into account.

Biocidal agent	Bacterial species with a strong and stable adaptive MIC increase
Benzalkonium chloride	*Enterobacter* spp. ($\leq$ 300-fold)
	E. coli ($\leq$ 100-fold)
	S. aureus ($\leq$ 39-fold)
	P. aeruginosa ($\leq$ 33-fold)
	A. baumannii ($\leq$ 31-fold)
Chlorhexidine digluconate	*E. coli* ($\leq$ 500-fold)
	S. marcescens ($\leq$ 128-fold)
	P. aeruginosa ($\leq$ 32-fold)
	K. pneumoniae ($\leq$ 16-fold)
	S. aureus ($\leq$ 16-fold)
Octenidine dihydrochloride	*P. aeruginosa* ($\leq$ 32-fold)



Kampf G (ed.). Antiseptic stewardship for wound and mucous membrane antiseptics. In: Antiseptic Stewardship: Biocide Resistance and Clinical Implications. Springer International Publishing, 2018; 689–694.

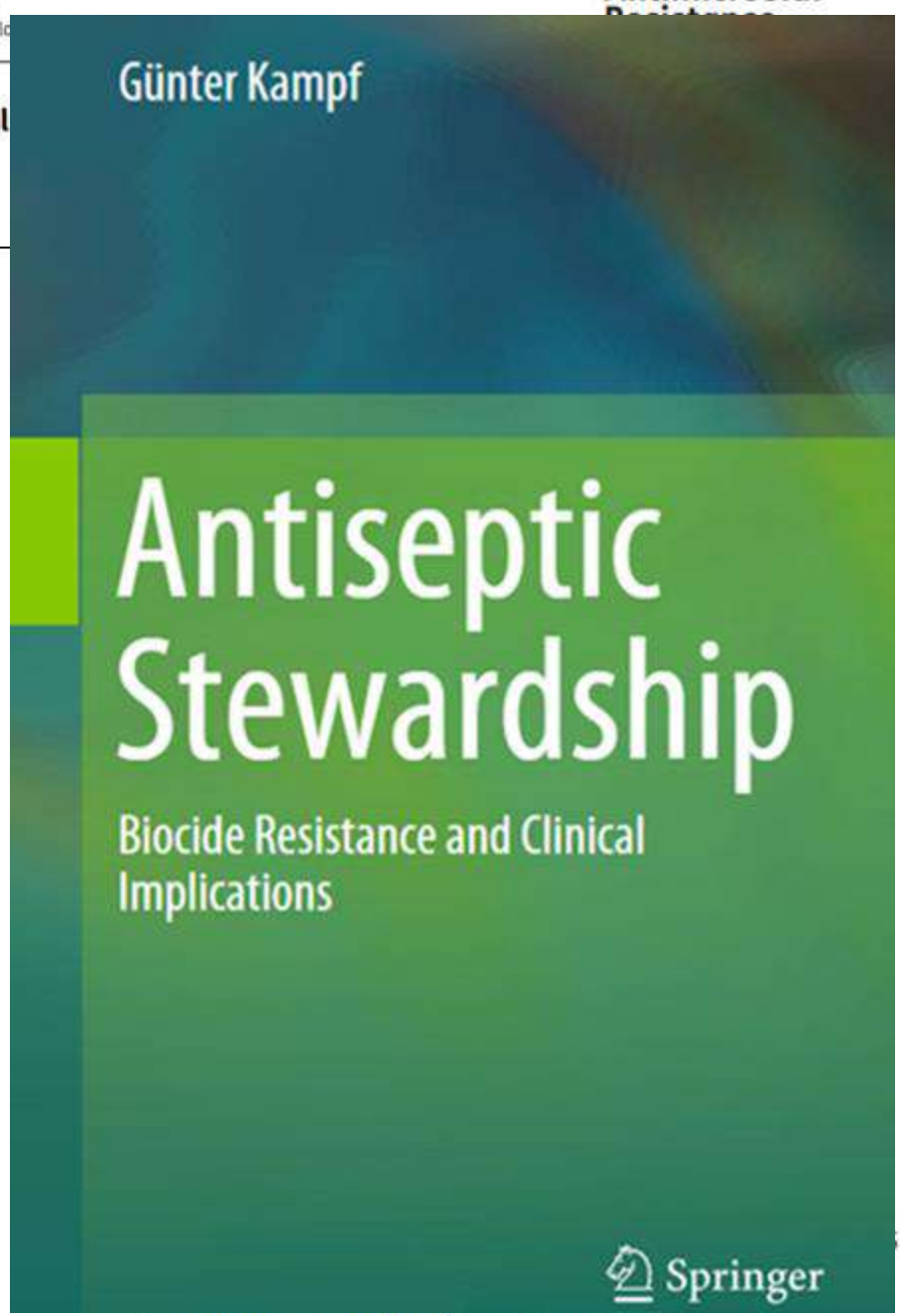
mycin (*P. aeruginosa*)

Antiseptikler ve Direnç

JAC Antimicrob Resist
doi:10.1093/jacamr/dl
JAC-Antimicrobial

Table 3. Antimicrobial efficacy of biocides used in wound dressings against biofilms

Examples of efficacy against bacteria in biofilm	Additional effect on biofilm
CHG	Silver/silver nanoparticles
• 500 mg/L CHG produced ≥4.2 log *S. aureus* within 5 min, but only a 1 min	• ≤3 log_{10} reduction of Ag^+/AgNP (0.01 and 25 mg/L) against *S. aureus* and mixed-species biofilms
• 1000–5000 mg/L CHG resulted in *Burkholderia cepacia* in 1 h	• 1.0 log_{10} reduction of AgNP (total Ag concentration: 27.3 mg/L; released Ag+: 1.5 mg/L) against *P. putida*
• 20 000 mg/L CHG resulted in ≤3 l 5 min	
• 20000 mg/L CHG resulted in ≤3 l 1 min whilst 200 mg/L 0.02% res *E. coli* in 2 h	OCT
• Up to 40 000 mg/L CHG resulted i *K. pneumoniae* or *P. aeruginosa* i	• 1% OCT produced >6 log_{10} reduction in bacteria in biofilm in 30 min for *A. viscosus*, *P. aeruginosa* and *S. aureus*
Povidone iodine/cadexomer	• 1% OCT produced 0.6–1.8 log_{10} reduction in *E. faecalis* and *Streptococcus mutans* in mixed-species biofilms
• 1% PVP-I resulted in ≥5.0 log_{10} r *S. haemolyticus*, *Staphylococcus xylosus* in a single-species biofilm 30 s or 1 min	Honey
• 7.5% PVP-I produced ≥5 log_{10} re 1 min and ≥5 log_{10} in *P. aerugino*	• Typical MBICs: 120 000–500 000 mg/L
• 2.5% PVP-I produced ≥5 log_{10} re *P. aeruginosa* in 24 h	• 5 log reduction after 24 h in *S. aureus*, *K. pneumoniae*, *P. aeruginosa*, *E. cloacae*, *A. baumannii*, *P. mirabilis* and *C. albicans*



Antiseptikler- *Candida auris*

Susceptibility of *Candida auris* and *Candida albicans* to 21 germicides used in healthcare facilities

William A. Rutala PhD, MPH[1], Hajime Kanamori MD, PhD, MPH[1,2,3], Maria F. Gergen MT (ASCP)[2],

Infection Control & Hospital Epidemiology (2019), 1–3
doi:10.1017/ice.2019.1

Table 1. Germicidal Activity Against *Candida auris* and *Candida albicans* Using a Quantitative Carrier Test Method

- 9 antiseptikten 7'sinde ***C. auris'e*** karşı 3-log10 azalma görülmedi

%10 povidon-iyot, %0,5 triklosan, %1 kloroksilenol, %1 klorheksidin glukonat (CHG) %61 etil alkol, %2CHG, %4 CHG ve %3 hidrojen peroksit !!

- Test edilen 13 dezenfektandan 10'u 1 dakikada en az 3-log10 azalma gösterdi,

  3 istisna hariç:

  (1) %5,25'lik sodyum hipokloritin 1:50 seyreltmesi

  (2) seyreltilmiş, su bazlı bir kuaterner amonyum bileşiği (QAC)

  (3) %0,55 orto-fitalaldehit (OPA)

				scrub/handwash		
Scrub-Stat 4%	Ecolab, St Paul, MN	4% chlorhexidine gluconate solution	Undiluted	Antiseptic/Surgical hand scrub/handwash	1.9	3.5
Isopropyl rubbing alcohol 70% USP	Medichoice, Mechanicsville, VA	70% isopropyl alcohol	Undiluted	Antiseptic/Disinfectant	3.8	4.1
Solution of hydrogen peroxide 3% USP	Medichoice, Mechanicsville, VA	3% hydrogen peroxide	Undiluted	Antiseptic	1.4	1.8

Antiseptikler- *Candida auris*

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William A. Rutala PhD, MPH[1], Hajime Kanamori MD, PhD, MPH[1,2,3], Maria F. Gergen MT (ASCP)[2],

- **Su bazlı bir QAC ve 1:50 oranında sodyum hipoklorit seyreltmesi hariç,**

hastanelerde kullanılan dezenfektanların çoğunun (13'ün 10'u, %77)

***C. auris'e* karşı etkili** (>3-log10 azalma)

- Yüzey dezenfektanı olarak yaygın olarak kullanılan **su bazlı QAC'lerin** sınırlı aktivitesi var!!
- *C. auris'li* hastaların bulunduğu odalarda çevresel yüzeylerin veya kritik olmayan hasta ekipmanlarının dezenfeksiyonu için QAC kullanılmamalı
- **%1,4 geliştirilmiş hidrojen peroksit ve alkol-kuaterner amonyum bileşikler**

***C. auris'e* karşı klor bazlı ürünler kadar etkili** olduğunu göstermektedir

Table 5. Bacteria-contaminating antiseptics, disinfectants, and hand hygiene products in healthcare facilities in high-income countries, for a total of 33 cross-sectional surveys that provided detail about both products and bacteria. Numbers represent the bacterial isolates, which outnumber the actual number of surveys since some surveys detected more than one contaminant. CHG = chlorhexidine gluconate, CNS = coagulase negative staphylococci, QUAT = quaternary ammonium compounds, PCMX = chloroxylenol.

Contaminating Bacteria	CHG Aqueous/Alcohol	QUAT/CHG–QUAT	Iodophor/ Iodine Tincture	Phenol [a]	Liquid Soap Antiseptic/Plain/ No Information	Bar Soap Antiseptic/ Plain	Total
Enterobacterales	**1/0**	**3/0**		**5**	**6/1/1**	**2/3**	**22**
Enterobacter spp.	-	-	-	-	1	-	1
Escherichia coli	-	-	-	2	1	2	5
Klebsiella spp. [b]	-	-	-	1	5	2	8
Serratia spp. [c]	1	2	-	2	1	1	7
Non-lactose-fermenting coliforms	-	1	-	-	-	-	1
Nonfermentative Gram-negative rods	**4/0**	**20/1**	**-**	**9**	**2/1/2**	**5/1**	**45**
Achromobacter spp. [d]	-	5	-	1	-	-	6
Acinetobacter calcoaceticus	-	-	-	-	-	1	1
Aeromonas spp.	-	1	-	-	-	-	1
Burkholderia cepacia complex	1	3	-	-	2	-	6
Flavobacterium spp.	1	-	-	-	-	1	2
Myroides odoratus	-	-	-	-	-	1	1
Pseudomonas aeruginosa	-	4	-	4	3	1	12
Pseudomonas spp. [e]	2	5	-	3	-	2	12
Stenotrophomonas maltophilia	-	1	-	-	-	-	1
Others	-	2	-	1	-	-	3
Gram-positive bacteria [f]	**0/1**	**0/1**	**2/2**	**-**	**9/0/0**	**7/7**	**29**
CNS/Micrococcus spp. [g]	1	1	4	-	4	5	15
Staphylococcus aureus	-	-	-	-	2	2	4
Gram-positive rods [h]	-	-	-	-	3	7	10
Yeast	**-**	**-**	**-**	**-**	**1/0/0**	**-**	**1**
Candida parapsilosis	-	-	-	-	1/0/0	-	1
Total	**5/1**	**23/2**	**2/2**	**14**	**18/2/3**	**14/11**	**97**

[a] Including hexachlorophene (n = 1), PCMX (n = 3) and phenol (n = 9). [b] *Klebsiella pneumoniae* (n = 1), *Klebsiella oxytoca* (n = 1), *Klebsiella* spp. (n = 4) and *Raoultella planticola/ornithinolytica* (n = 2). [c] Including *Serratia marcescens* (n = 6) and *Serratia* spp. (n = 1). [d] Given the difficult phenotypic identification and the changes in classification (*Achromobacter xylosoxidans* has been temporarily classified to the *Alcaligenes* genus) [37], both *Achromobacter* and *Alcaligenes* species were lumped as *Achromobacter* spp. [131]. Species names listed in the articles include *Achromobacter xylosoxidans* (n = 3), *Achromobacter* spp. (n = 2), and *Alcaligenes faecalis* (n = 1). [e] Including *Pseudomonas* spp. (n = 8), *Pseudomonas putida* (n = 2), *Pseudomonas fluorescens* (n = 1) and *Pseudomonas chlororaphis* (n = 1). [f] Nine bacterial isolates (5 CNS, 3 *Micrococcus* spp. and 1 *Staphylococcus aureus*) detected by filtration of 100 mL of product, a maximum colony count of 3 colonies in 100 mL. [g] Including CNS (n = 10) and *Micrococcus* spp. (n = 5). [h] Including *Bacillus* spp. (n = 3), *Corynebacterium* spp. (n = 2), *Cutibacterium acnes* (n = 4) and *Nocardia* spp. (n = 1).

pumps, see Barsaghi et al. [36].

Özet

- **Hipokloröz asit çok hızlı etki ettiği ve her dokuda güvenle kullanılabildiği için iyi bir seçenek ama etkisi kalıcı değil**
- **Oktenidin yara tedavisinde hızlı ve uzun etkili olması nedeniyle iyi bir seçenek ancak basınçlı kullanımda doku hasarı riski var**

Yeni antiseptiklere ihtiyaç devam ediyor

Antiseptiklerde direnç gelişimi gelecekte büyük sorun olabilir

Antiseptik kontaminasyonu ile salgın olabilir

Yılmak Yok Yola Devam
Hep Birlikte Yaralarımızı Sarabiliriz

Tablo 21.2 Antiseptiklerin karşılaştırılması

Grup Gram	Gram Pozitif Bakteri	Gram Negatif Bakteri	Mikobakteri	Mantar	Virüs	Etki hızı
Alkoller	+++	+++	++	++	+	Hızlı
İyod bileşikleri	+++	+++	+++	++	+++	Orta
İyodoforlar	+++	+++	+	++	++	Orta
Klorheksidin (%2 ve %4)	+++	++	-	+	+	Orta
Polihekzametilen biguanid	+++	+++	?	++	++	Orta
Oktenidin	+++	+++	?	+++	++	Hızlı
Hekzaklorofen	+++	+	+	+	+	Orta
Triklosan	+++	++	+	--	+++	Orta
Dörtlü amonyum bileşikleri	++	+	-	++	++/-	Yavaş
Hipokloröz asit	+++	+++	+++	+++	+++	Hızlı
Hidrojen peroxid (%3)	+++	++	+	+	++	Hızlı