# MARKET AND BUSINESS POTENTIAL ANALYSIS OF WOUND HEALING PRODUCTS OF DERMOBOR

by Berfu Tavelli

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APPROVED BY:

Prof. Dr. Fikrettin Şahin (Thesis Supervisor) (Yeditepe University)

Prof. Dr. Ahmet Çağrı Büke (Yeditepe University)

Prof. Dr. Gülden Zehra Omurtag (Medipol University)

Aundali

agu Jars

DATE OF APPROVAL: ..../2019

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### ABSTRACT

## MARKET AND BUSINESS POTENTIAL ANALYSIS OF WOUND HEALING PRODUCTS OF DERMOBOR

Acute and chronic wounds are critical medical problems throughout the world due to leading serious mortality and morbidity along with economic burden. Acute wounds do not always need professional treatment, but chronic wounds are mainly accompanied by infection resulted in continuous tissue degradation. There are variety type of wound healing products performed according to the severity of the wound at the moment. Boron containing product Dermobor demonstrated the wound healing effect in vivo and in vitro wound model and it has been newly launched in Turkey. Dermobor enhances acute cutaneous wound healing by preventing infections in wound areas, and increasing fibroblast migration, antioxidant enzyme activity, growth factor expression levels. Carbopol-based hydrogel formulated with boron and pluronic block copolymers is also effective for burn wound management with its enhanced epithelization, wound closure, and angiogenesis feature. Treatment with Dermobor also successfully diminished radiation-induced skin reactions. In this study, Dermobor business and market potential researched based on acute and chronic wound healing product sales that has been already in the market. Topical antibacterials, dermotolgical preparation, antiseptics and wound healing ATC classification has been analyzed in this study utilized from IQIVIA databases. The made-up market consisting from those products has increased 18 percent its value and reached 258 million Turkish Lira in 2018. Considerin the same market for the world data of those market costs 3 billion Euro in value. Consumer behaviour in the pharmacy to the selection a product from those market has been commented on the result of online survey which has 381 respondents. Dermobor positioned as a wound healing product which regenerates tissue and stimulates the healing of: ulcers, wounds, fistulas, burns, inflamations, surgery, grafting, radioepitelitis in various medical specialties.

## ÖZET

# YARA İYİLEŞTİRİCİ DERMOBOR ÜRÜNÜNÜN PAZAR POTANSİYEL ANALİZİ

Akut ve kronik yaralar ciddi hareket kısıtlılıklarına ve ölümlere yol açtığı için dünyaya ekonomik yük getiren önemli bir medikal problemdir. Akut yaralar genellikle profesyonel bir tedavi yaklaşımı gerektirmezler ama kronik yaralara çoğunlukla enfeksiyon, uzun süreli iltihaplanma eşlik eder ve iyileşme süreci bozulur ve doku degradasyonuna yol açılır. Bu nedenle yeni, güvenli etkili yara iyileştirici ürünler uluslararası çalışmalarda her zaman ilgi çekici bir alan olmaktadır. Şu anda pazarda yaranın şiddetine göre tedavide değişiklik gösteren farklı ürünler bulunmaktadır. Boron içeren Dermobor ürünü in vitro ve in vivo çalışmalarıyla yara iyileşmesinde etkili olduğunu kanıtlamıştır ve Türkiye'de piyasaya sunulmuştur. Dermobor akut deri yarası iyileşmesi sırasında gerçekleşen enfeksiyonların fibroblast migrasyonunu, antioksidan enzim aktivitesini, büyüme faktörü kontrolü, expression miktarını artırarak yaranın iyileşmesini artırır. Dermobor aynı zamanda epitilizasyonu arttırma, anjiyogenezi hizlandırma özellikleriyle yanak yara yönetiminde de etkilidir. Dermobor tedavisinin radyasyona bağlı yara reaksiyonlarında da etkili olduğu yapılan çalışmalarla gösterilmiştir. Bu çalışmada Dermobor, pazar potansiyeli akut ve kronik yaralar için pazarda kullanılan ürünlerin satışlarına göre değerlendirilmiştir. Topikal antibakterial, dermotolojik ürünler ve yara iyileştirici ürünlerin satışları dünya sağlık örgünün ATC sınıflandırılmasına dayanarak IQIVIA databasinden elde edilmiştir. Pazarların birlikte analizi soncunda 2018 yılında bu ürünlerin satışlarının bir önceki yıla oranla yüzde 18 büyümüş olduğu ve 258 milyon Türk Lirasına ulaşmış olduğu gösterilmiştir. Aynı Pazarın 34 ülkeden oluşan dünya datasına baktığımızda bu pazarın 3,5 bilyon Euro değerinde olduğunu görmekteyiz. Eczanede bu olandaki ürün seçimindeki tüketici davranışlarının sorgulandığı online arnketi 381 kişi cevaplamıştır. Tüm bu araştırmalar sonucunda Dermobor doku yenilenmesini sağlayan ve yaranın iyileşmesini düzenleyen bir yara iyileştiri ürün olarak ülcerlerde, fistüllerde, yanıklarda, ödemlerde, operasyonalardan sonra yara iyileşmesinde konumlandırılmıştır.

# TABLE OF CONTENTS

ACKNOWLEDGEMENTS	III
ABSTRACT	IV
ÖZET	v
LIST OF TABLES	VII
LIST OF SYMBOLS/ABBREVIATIONS	IX
1. INTRODUCTION	1
1.1. AIM OF THE THESIS	2
1.2. LITERATURE REVIEW OF WOUND HEALING	2
1.2.1. The Physiology of Chronic Wound	3
1.2.2. Chronic Wound Classification and Theraphy	5
1.2.3. Chronic Wound Healing Theraphy Costs	9
1.3. DERMOBOR	
2. MATERIALS AND METHODS	13
3. RESULTS	14
3.1. SALES ANALYSIS OF WOUND HEAILING PRODUCTS	14
3.2. PRESCRIPTION ANALYSIS OF WOUND HEAILING PRODUCTS	26
3.3. STAKEHOLDER ANALYSIS OF WOUND HEALING PRODUCTS	27
3.4. CONSUMER BEHAVIOUR ANALYSIS	
4. DISCUSSION	
5. CONCLUSION	32
REFERENCES	33

# LIST OF TABLES

Table 1.1. Factors affecting wound healing ability    3
Table 1.2. Types of common chronic wounds and their specific therapy
Table 1.3. Standard treatment of diabetic foot according to Wagner classification
Table 1.4. Wound cleansing products in Turkey    8
Table 1.5. Pressure ulcer per person average therapy expenses in Turkey
Table 1.6. The average annual cost per patient in diabetic foot treatment
Table 3.1. Dermobor retail market potential analysis    14
Table 3.2. Topical antibacterials retail sales value analysis in TL    14
Table 3.3. Antiseptics and disinfectants retail sales value analysis in TL
Table 3.4. Other wound healing agents retail sales value analysis in TL
Table 3.5. Topical antiviral retail sales value analysis in TL    25
Table 3.6. Other dermatological preperation retail sales value analysis in TL21
Table 3.7. Retail and hospital wound healing sales value analysis in TL
Table 3.8. World sales analysis of the related market in Euro    25
Table 3.9. Wound healing agents prescription market data vs. specialities
Table 3.10. Topical antibacterials prescription market data vs. specialities

Table 3.11. Other dermatological prep prescription market data vs. specialities	26
Table 3.12. Wound and diabetic foot council unit in Turkey	27
Table 3.13. Key opinion leader in Turkey	28
Table 3.14. First chosen brand of consumer for burn wound	28
Table 3.15. First chosen brand of consumer for Herpes Simplex	29
Table 3.16. Comments on triple effect for a brand	29

# LIST OF SYMBOLS/ABBREVIATIONS

ATC	WHO the anatomical therapeutic chemical		
ECM	Extracellular matrix		
FGF	Fibroblast growth factor		
PEDIS	Perfusion, extent, depth, infection and sensation		
PMN	Polymor phonuclear leukocyte		
TGF	Transformation growth factor		
TNF	Tumor necrosis factor		
TRH	Trainee and research hospital		
VEGF	Vascular endothelial growth factor		
ROS	Reactive oxygen species		
MMP	Matrix metalloproteinase		
LEMAs	Lover extremity major amputations		
DM	Diabetes mellitus		
PDGF	Platelet-derived growth factor		
DFU	Diabetic foot ulcers		
PU	Periferic ulcers		
IL	Interleukin		
WBP	Wound bed preperation		

## **1. INTRODUCTION**

Wound healing has been recognized as important to health since the beginning of mankind. After 5,000 years, the goals for wound theraphy have not changed. The patient still deserves a fast, uncomplicated and antiseptic wound closure, but also claims an aesthetic outcome with unimpressive scar formation. Acute wound healing typically progresses through four stages over approximately 8 to 12 weeks. However, if healing stalls in one of these phases, the wound may become chronic [1]. Chronic wounds can be accompanied with infection and prolonged inflammation resulted in continuous tissue degradation. They are critical medical problems throughout the world due to leading serious mortality and morbidity along with economic burden [2]. Age, immune status, malnutrition, infection, insufficient oxygenation or perfusion, smoking, diseases, medications, radiation, and chemotherapy are the main risk factors that can lead to chronic wound formation [3]. Chronic wounds are defined as vascular ulcers, diabetic ulcers, and pressure ulcers [4]. Life-threatening infections, extremity amputations or severely reduced health conditions due to these chronic wounds are still the major challenges of the current technology. A variety of wound dressings include transparent films, hydrocolloids, foams, alginates, gels, and collagen-based products to keep the wounds moist because it is reported that the moist wounds heal faster. Chronic wounds bring ischemia, pressure, and infection. Wound healing process is directly related with these factors. Wound healing products in the market claim a better optimization locally and systemically and they also insist on providing an ideal wound healing environment, but they do not meet the expectations due to being high-priced and not easily attainable, requiring wound care facilities, having patient-specific response, low efficiency and severe sideeffects. In this sense, developing new, safe, self-applicable, effective and cheap wound care products with broad-range antimicrobial activity is still an attractive area of international research due to an increasing elderly population and the subsequent increase in chronic diseases such as diabetes [2].

#### 1.1. AIM OF THE THESIS

The purpose of this thesis is to investigate the business potential of Dermobor products in the specialized market. Dermobor has recovering effect on acute and chronic wound. Because it has an antiviral effect, it has an healing effect also for the herpes simplex. People do not visit to the physician for the mild wounds. They can buy one of the topical medication generally while consulting to the pharmacists. They may prefer particularly a product that they heard before one of their acquaintance. An online perception market research showed us the consumer's most preferred products for the burn wound, wound healing and herpes simplex. Prescription products according to specialities documented to understand whih specialities choose which product. A corelation between physician's prescription and consumer mind could be established. Dermobor will have new indication in the coming years. The thesis will support the product postioning and strategy of Dermobor.

#### **1.2. LITERATURE REVIEW OF WOUND HEALING**

The skin is the largest organ of man and serve lots of fuction so healing of a skin wound exhibits cascading cellular function system extraordinally that is unique in nature. Wounds are classified by their aetiology, location, type of injury or presenting symptoms, wound depth and tissue loss or clinical appearance of the wound. Separate grading tools exist for Pressure Ulcers (EPUAP), Burns (Rule of Nines), Diabetic Foot Ulcers (Wagner / San Antonio) and General Wounds. General wounds are classified as being superficial, partial thickness and full thickness.

Area	Factors	
	Aetiology	
	Co-morbidity e.g. diabetes mellitus, auto-immune disease	
	Nutritional Status	
Patient	Allergy	
1 attent	Medication e.g. steroids	
	Psychosocial status	
	Pain	
	Concordance	
	Duration	
	Size	
	Wound Bed Condition	
Wound	Ischaemia	
	Inflammation/infection	
	Anatomical Site	
	Treatment Response	
Care Provision	Healthcare system	
	Skill and knowledge	

Table 1.1. Factors affecting wound healing ability [5]

#### 1.2.1. The Physiology of Chronic Wound

Wound healing is a process of replacing and restoring of the damaged skin. It can be divided physiologically into four dynamic phases: Coagulation, inflammatory, proliferating and remodelling [Table 1]. The function of the coagulation pathway is to keep hemostasis, which is characterized by vasoconstriction and blood clotting. Platelets secrete growth factors and cytokines attract fibroblasts, endothelial cells, and immune cells to initiate the healing process. The life-saving vasoconstriction with clot formation accounts for a local perfusion failure with a consecutive lack of oxygen, increased glycolysis and pH-changes. The vasoconstriction is then followed by a vasodilation in which the traumatized tissue suffers a reperfusion phenomenon [6]. The dominant cells of the inflammation phase are neutrophils and macrophages. Neutrophils release reactive ROS to prevent bacterial contamination and remove cellular debris. Blood monocytes migrate to the wound area and differentiate into tissue macrophages. In order to stabilize damaged blood vessels, macrophages dissolves various growth factors and cytokines that invoke fibroblasts, endothelial cells and keratinocytes. Inflammatory phase takes up to 7 days when the it ends, it results in apoptosis

of immune cells and the proliferation phase begins. This phase is mainly defined by tissue granulation, formation of new blood vessels (angiogenesis) and epithelization. The final stage occurs after the wound closes and may last for 1-2 years or longer. At this stage, the transient matrix is reconstructed into organized collagen bundles [7,8]. Chronic wounds are defined as non-treated wounds that has not normal stages of wound healing for the time and sequence manner. Generally, chronic wounds stop at the stage of inflammation. Comparing the characteristics of an acute healing wound with the chronic one allows you to gain an indepth understanding of the underlying molecular and physiological deterioration of nonhealing wounds. Despite differences in the etiology at the molecular level, chronic wounds share certain common features such as excessive proinflammatory cytokine levels, proteases, reactive oxygen compartments and aging cells, the presence of persistent infection, and the insufficiency of stem cells. Microorganisms and platelet-derived factors stimulate the immune cells constantly. In acute wounds, proteases are tightly regulated by their inhibitors. In chronic wounds, protease levels exceed the level of their inhibitors, causing destruction of ECM and degradation of growth factors and receptors. The proteolytic destruction of the ECM not only prevents the wound from progressing to the proliferative phase, but also attracts more inflammatory cells, thereby enhancing the inflammatory cycle [9]. Immune cells produce ROS that defense against microorganisms at low concentrations. However, the predominant hypoxic and inflammatory environment increases the production of ROS In chronic wounds, which harms ECM proteins and hence causing cell damage. This sequence of events leads to an enhanced stimulation of proteases and inflammatory cytokines [10]. While the intake of potent antioxidants reduces ROS to normal levels, chronic wounds may reverse and improve healing [11]. In addition, chronic wounds are characterized by aging cell populations with proliferative and secretory capacities diminish, and do not respond to typical wound healing signals [12]. Fibroblasts from venous and peripheral ulcers are old and has less ability to proliferate [13-15]. This decreased proliferative capacity is directly related in non-healing of a wound. Collected data indicate that chronic wounds contain aged keratinocytes, endothelial cells, fibroblasts, and macrophages [15-18]. In chronic wounds, the cell phenotype associated with stopping the cell cycle due to DNA damage, while causing problems in intracellular biochemical pathways [17,19]. All possible factors and cofactors that may influence healing must be identified. Due to the multifactorial nature of chronic wounds, the molecular environment of chronic wounds contains elevated levels of inflammatory cytokines and proteases, low levels

of mitogenic activity, and cells that often respond poorly to growth factors compared to acute healing wounds.

Phase	Timing	Cellular Events	Mediators
Coagulation	0–3 d	Vasoconstriction and	Thromboxane A2;
		platelet aggregation	serotonin and
			adrenalin; and
			coagulation cascade
Inflammatory	1–3 d	PMNs, monocytes,	PDGF, VEGF, and
		macrophages, and	TGF-α; TGF-β; TNF-
		lymphocytes	α; MMPs; FGF; and
			IL-1 and IL-6
Proliferating	4 days to weeks	Fibroblasts, ECM	Collagen type 1, 3
		deposition,	deposition; VEGF;
		epithelialization, and	and PDGF
		angiogenesis	
Remodeling	Weeks to months;	Remodeling, wound	Increase in type 1
	occasionally years	contraction, and	collagen and increased
		myofibroblasts	collagen cross-linking

Table 1.2. Phases of the wound healing table [1]

#### 1.2.2. Chronic Wound Classification and Theraphy

The treatment process of chronic wounds is not only eliminate the etiological causes, but also to terminate underlying systemic and metabolic deteriorations. The first step of wound assessment start with the initial encounter with patient while considering the patient's living situation and the possible effect of a given drug on patients. These two factors determine the therapies to heal the wounds. WBP requires a comprehensive, well-coordinated and sometimes multidisciplinary approach. It aims to remove the factors which impede in tissue regeneration while favouring endogenous healing, promoting cellular proliferation and the reparatory processes "triggered" by the products applied. The Wound Healing Association has encouraged the use of the TIME acronym to comprehensively identify, communicate and address the main elements of chronic wound healing so it outlines the principles of WBP. TIME divided to the parts of a single treatment process, showing the basics to be addressed during the preparation of the wound bed. T is for tissue represents the determination of the

presence of destructive or necrotic tissue and identification of specific deficits. I for inflammation or the presence of infection or both. M describes the state of the moisture balance. E indicates the edge of the wound, whether it is progressive or weakened, or at the extent of re-epithelialization [20].

Common Types	Pathology	Specific Theraphy
Venous Ulcer	Deep venous insuffi ciency, post thrombotic syndrome, primary varicosis	Graduated compression bandaging (if ABI $>0.6$ ), physical activity, elevation, pain assessment, superficial vein surgery (with compression)
Arterial Ulcer	Macroangiopathy	Angioplasty, major vascular surgery, pharmacological improvement of blood flow, physical activity, reduction of risk factors
Diabetic Ulcer	Neuropathy, small-vessels disease	Glycaemic control, off -loading or orthopaedic footwear, therapy of possible arterial or venous insufficiency
Mixed Ulcer	Venous/arteria	Under venous and arterial ulcer
Pressure Sore	Immobility, neuropathy	Mobilisation and positioning, pressure-relieving support surfaces, nutritional support, surgical intervention

Table 1.3. Types of common chronic wounds and their specific therapy [21]

It can be struggle to select the exact category of the wound accurately based on the assessment of the contamination level and the duration of injury. Downgrade the wound's classification is better option in case of doubt. Early action can reduce the likelihood of infection. Diabetic foot ulcers class and its treatment algorithm can be understood with the Wagner classification. The ischemic index is a basic value for predicting diabetic ulcer healing [22].

Grade-0	Foot at Risk	Prevention
Grade-I	Localized, superficial ulcer	Antibiotics and glycemic control
Grade-II	Deep ulcer to bone, ligament, or joint	Debridement, antibiotics and glycemic control
Grade-III	Deep abscess, osteomyelitis	Debridement, some form of amputation
Grade-IV	Gangrene of toes, forefoot	Wide debridement and amputation
Grade-V	Gangrene of entire foot	Below knee amputation

Table 1.4. Standard treatment of diabetic foot according to Wagner classification [23]

Table 1.5. PEDIS<sup>a</sup> grades and treatment paradigms [24]

Grade	Infection Severity	Clinical Manifestations	Medications
1	Uninfacted	Wound without purulence or inflammation	Topical Antibiotics
2 <sup>b</sup>	Mild	<ul> <li>≥2: purulence or erythema, pain, tenderness, warmth, or induration; cellulities ≤2 cm around ulcer; infection limited to skin/subcutenous tissue; no othercomplications</li> </ul>	Cephalexin, TMP-SMX ,levofloxacin, amoxicillin and clavulanate, clindamycin
3°	Moderate	Infection as above >1; cellulities >2 cm, streaking, deep tissue abscess, gangrene and with some life-threatening; involment of muscle, tendon, joint or bone	TMP-SMX, amoxicillin and clavulanate, levofloxacin, ceftriaxone, linezolid, ertapenem, ticarcillin clavulanate
4 <sup>d</sup>	Severe	Infection plus systemic toxicity or metabolic instability; fever, chills, tachycardia, hypotension, confusion, vomiting, severe hyperglycemia, acidosis, or azotemia	Imipenem cilastatin, vancomycin ceftazidime, levofloxacin clindamycin, piperacillin tazobactam,

		ticarcillin clavulanate

<sup>a</sup> PEDIS stands for perfusion extent or size depth or tissue, loss infection and sensation <sup>b</sup> Medication of treatment can be oral

<sup>c</sup> Mediation for treatment can be oral or parental, based on clinical situation <sup>d</sup> Mediation for treatment are IV, at least initially

Multiple treatment modalities including exogenous growth factor applications, tissueengineered skin substitutes, electrical stimulation, hyperbaric oxygen therapy, negative pressure therapy, chemical formulations are being used in current dermatology. Altough they defend to serve better optimization locally and systemically, they fail due to high price and not easily reachable, need facilities, differentiate according to the patient type, less efficiency, and serious side-effects [25].

## 1.2.2.1. Cleansing

Wound cleansing products should be a neutral, nonirritating, nontoxic solution. Mild soap can be used if it is not perfumed, without antibacterials and at skin pH: 4.5-5.7. In addition to that water can be also good solution for cleansing. They are effective, safe and cheap. Wound antiseptic agents, e.g. hydrogen peroxide, hypochlorite solution, acetic acid, chlorhexamide, providone/iodine, cetrimide and others have antibacterial properties, but are all toxic to healthy granulation tissue [26].

Products and Company	Form	Active Ingredient	Positioning
Crystalin Dermal Sprey	100	Hypochlorous Acid	Biofilm eradication
NHP Pharma	ml/bottle		Wound healing by
			activation fibroblasts

Crystalin Antiseptic Spray NHP Pharma	200 ml/bottle	Hypochlorous Acid	and keratinocyte Broad spectrum antimicrobial activity
Crystalin Liquid Solution NHP Pharma	ml/bottle	Hypochlorous Acid	
Octenispt Solution Farmakim	1000 ml/bottle	Octenidine dihydrochloride %0,1 Phenoxyethanol %2	Broad antiseptic spectrum of activity Well tolerated by skin and mucous membrane Painless application Suitable for infants and premature babies
Prontosan Solution	1000	0.1 %	Reduces healing time
BBraun	ml/bottle	Polyaminopropyl Biguanide (Polihexanide)	Removes and prevents the formation of biofilm Prevents infections
Silgen Wound Spray Genadyn	1000 ml/bottle	Novel Nano-colloidal Silver at above 30ppm	Antimicrobial effect Reducing the use of antibiotics

#### 1.2.2.2. Debridement

Debridement is the removal of unhealthy tissue from a wound to promote healing. The types of debridement are surgical, chemical, mechanical, or autolytic removal of the tissue. Biologic debridement is the use of living organisms to remove necrotic or dead tissue from a wound. Enzymatic Debridement uses naturally occurring proteolytic enzymes produced by the pharmaceutical and healthcare industry specifically for eliminating remove foreign bodies and tissue that has become necrotic. Hydrocolloids, hydrogels, and transparent films are commonly used dressing types. On the other hand, mechanical debridement is facilitated for healing moist wound while removing drainage and dead tissue from wounds [27].

#### 1.2.3. Chronic Wound Healing Theraphy Costs

Each year 2.5 percent of patients with diabetes will have by diabetic foot ulcers, and that 15 percent of patients with diabetes will ultimately be affected by diabetic foot ulcers [28,29]. The incidence of foot problems ranges from 10 percent to 25 percent throughout the lifetime of a Diabetes mellitus (DM) patient [30-32]. 400.000 DFU cases can be shown in Turkey,

and 7700 amputation surgery are realized annually due to DFU [22]. Mortality after amputation are changed from 13 to 40 percent in 1 year, 35-65 percent in 3 years, and 39-80 percent in 5 years. [33]. The point prevalence of PU in a sample university hospital in Turkey was 10.4 percent [34].

The health economics survey defines costs in two main categories. The first is the medical costs incurred by the disease, and the second is the costs associated with the other disease, including non-medical costs incurred by the disease. There are direct and indirect costs in each category. Direct costs indicate which payments are made and indirect costs indicate which resources are lost. Direct medical costs consist of all types of exclusive and non-exclusive uses of resources. Indirect costs are morbidity and mortality costs [35-39].

Pressure Ulcer Per Person Average Costs	Dolar (\$)
Per Person Antibiotic Cost	796
Per Person Feeding Cost	176
Per Person Total Medical Treatement Cost	973
Per Person Debridement Cost	5,8
Per Person Flap Cost	19
Per Person Microbiology Culture Test Cost	0,3
Per Person Dressing Cost	20,1
Per Person Surgery Wound Care Cost	45,4
Per Person Daily Cost For Hospital Stay	71
Per Person Daily Total Cost	211,4
Per Person Daily Total Hospital Stay	3.512
Per Person Daily Total Cost	4.615

Table 1.7. Pressure ulcer per person average therapy expenses in Turkey [40]

at 16.11. 2015, 1 dollar = 2,88 TL

#### **1.3. DERMOBOR**

Boron is one antioxidant agent that can stop oxidative damage by increasing the levels of glutathione and its derivatives, or scavenging anti-reactive oxygen species (ROS) [41, 42]. The wound healing effects of boron compounds were previously demonstrated in *in vivo* and *in vitro* wound models [43–46]. Dermobor includes 0.2 percent Chlorhexidine Digluconate

as an active material and 3 percent Sodium Pentaboratepentahidrate co-formulated with poloxamers (F68 and F127). Sodium Pentaborate pentahidrate is the active compound for wound healing properties and inhibits microbial growth in the wound tissue together with Chlorhexidine. Poloxamers, known as pluronics or kolliphors, are nonionic and amphipathic triblock copolymers can form micelles and hydrogels at above critical gel concentrations, under proper conditions [47]. F68 and F127, have been shown to be effective in wound healing themselves, by inhibiting inflammation and stimulating growth factor expression [48, 49]. It shows the highest activity, especially against Staphylococcus aureus, Yersinia enterocolitica, Candida albicans, Candida glabrata, and Aspergillus niger. Pluronics increases the antimicrobial activity and wound healing by enhancing cellular uptake, transport through the membrane and promoting cell proliferation [50]. Sodium pentaborate pentahydrate combined with pluronics has increased migration, superoxide dismutase activity, and vital wound healing-associated gene expressions of primary human fibroblast cells in vitro along with augmenting collagen deposition and wound contraction in vivo. Dogan et al. showed that sodium pentaborate significantly increases wound healing by increasing the migration capacity and superoxide dismutase activity of primary human fibroblasts in vitro and in vivo. It increased the antioxidant enzyme activity with increasing Superoxide dismutase activity. It also increased gene expression levels of important genes in fibroblast cells VEGF, TNF- $\alpha$ , and TGF- $\beta$  mRNA levels. TGF- $\beta$  is the critical mRNA manages nearly each phase of the wound healing process. It mediates fibroblast migration, inflammation, angiogenesis, cell proliferation, extracellular matrix production. VEGF expression has a mission as a pro-angiogenic factor. TNF- $\alpha$  levels might be related with pro-inflammatory actions [49].

Thickness of epidermis and granulation tissue, inflammatory cell infiltration, fibroblast proliferation and collagen deposition are associated with the wound healing properties. Dermobor enhances acute cutaneous wound healing by increasing fibroblast migration, antioxidant enzyme activity, growth factor expression levels. Enhanced epithelization, wound closure, and angiogenesis is promising for an effective burn wound management [56]. It is showed that Dermobor with its unique formultaion is highly effective product against virus, bacteria, yeast and fungal diseases. It is particularly influential to treat various kinds of wounds, in particular diabetic foot ulcer, decibitus ulcer and excudates wounds.

According to the result of the study which is conducted by Cagri Buke with Diabetic Foot Infection patients in a 57 years old, the complete clousure of the wound acted in 50<sup>th</sup> days with using Dermobor gel treatment twice a day. The other 72 years old female patient's wound closure completed in 16<sup>th</sup> days [50].

Wound Types	Days of Treatment
Diabetic Foot Ulcer	3 <sup>th</sup> week
Venous Ulcer	9 <sup>th</sup> week
Empirical Case Bedsore	11 <sup>th</sup> week
Foot Wound	4 <sup>th</sup> week

Table 1.8. Days of treatment of chronic wounds with dermobor gel treatment

A phase 1 clinical trial to observe the foot wound's recovery in the diabetic and peripheral arterial or venous insufficiency patients has been started on September 2015 in responsibility of Prof. Dr. Erhan Aysan who is the member of SB Istanbul Education and Research Hospital. In thic clinical trials, Dermobor has been applied to the first group after wound dressing and hydrogel without any active ingredient has been applied for the control group everyday for two months. The same doctor observed and took photo of the wounds every week in the outpatients clinic. The estimated completion date of this clinical trial is on December 2023 [51].

Erhan Aysan et all. researched also to assess boron effects on radiation-induced skin reactions (RISR) results from an adverse effects of external radiotherapy in breast cancer patients. Treatment with a boron-based gel successfully decreased radiation-induced skin reactions (RISR) but nearly 1/3 of the patients had grade >2 RISR. Different boron doses and combinations with other topical agents are necessary [52].

## 2. MATERIALS AND METHODS

The Anatomical Therapeutic Chemical (ATC) Classification system was developed a tool to make better quality of drug benefit. In the ATC Classification, drugs are seperated into different class according to the organ or system on which they have effect and their chemical, pharmacological, and therapeutic qualities therefore drugs could be compared at international, national or local levels. The Market of Dermobor has been defined according to the ATC classification [53]. IQVIA database for sales and prescription information has been used to get an insight. Dermobor has not been sales data on IQVIA database yet. IQVIA sources information from more than 550 suppliers including nearly 100 pharmaceutical manufacturers. It may be the reason that those suppliers wouldn't include one of the sales channels of Dembor. Retail and hospital sales analysis and prescription analysis dashboard used to assess the business potential of Dermobor.

RxMediaPharma is an online interactive drug information resource. Used by many hospitals and over 20,000 retail pharmacies and medical clinics in Turkey as well as government and Social Security Institution (SGK), pharmaceutical manufacturers and academic institutions. Rx MediaPharma is used to competitor analysis.

Dermobor has high probability to be a member of D03A9 other wound healing agent market. Morever, the topical antibacterials D06A0, antiseptics and disinfectants D08A0 and other dermatological preperation market D11A0 have been also analysed to have broader insight because Dermobor can be also used instead of the products that belongs to these markets.

It has been conducted also a secondary market research as a online survey to understand the consumer behaviour with the perception analysis. The questions have been conducted with a three question and they were placed on a reputable survey tool, "SurveyMonkey". The survey opened on 19<sup>th</sup> of July 2019 and closed one month later. 381 respondats' insights have been assessed. The answers stemming from the survey results could help drive Dermobor future brand marketing strategy [54].

## **3. RESULTS**

#### 3.1. SALES ANALYSIS OF WOUND HEAILING PRODUCTS

IQVIA database for sales and prescription information has been used to get an insight mainly in the market of D03A9 other wound healing agent market. Morever, the topical antibacterials D06A0, antiseptics and disinfectants D08A0 and other dermatological preperation market D11A0 have been also analysed to have broader insight. The data includes both retail and hospital market.

Table 3.1. Dermobor retail market potential analysis [55]

DERMOBOR RETAIL MARKET POTENTIAL	TL Year/18
D11A0 OTHER DERMATOLOGICAL PREP	38.532.942
D06A0 TOPICAL ANTIBACTERIALS	90.003.700
D08A0 ANTISEPTICS+DISINFECTANTS	32.006.143
D03A9 OTH WOUND HEALING AGENTS	97.692.546
TOTAL MARKET	258.235.331

Table 3.2. Dermobor retail and hospital total market potential analysis [55]

DERMOBOR RETAIL and HOSPITAL MARKET POTENTIAL	TL Retail and Hospital Price Year/18
D03A9 OTH WOUND HEALING AGENTS	103.178.126
D06A0 TOPICAL ANTIBACTERIALS	94.176.882
D11A0 OTHER DERMATOLOGICAL PREP	38.553.296
D08A0 ANTISEPTICS+DISINFECTANTS	34.753.355
TOTAL MARKET	270.661.659

Table 3.3. Topical antibacterials retail sales value analysis in TL [55]

PRODUCT NAME	TL YTD/6/2019	TL Year/16	TL Year/17	TL Year/18
TOTAL MARKET	59.083.688	60.972.644	76.209.186	90.003.700
FUCIDIN	12.929.375	13.583.206	16.265.320	20.937.429

			44.0.00.000	1
CREAM 2 % 1 20 G	9.651.201	9.622.326	11.968.660	15.661.486
OINT 2 % 1 20 G	3.278.174	3.960.880	4.296.660	5.275.943
TERRAMYCIN	12.203.775	8.034.028	15.353.744	15.308.420
OINT 1 14 G	12.203.775	8.034.028	15.353.744	15.308.420
BACODERM	6.211.578	7.017.202	5.477.890	11.337.629
OINT 2 % 1 15 G	3.272.003	4.553.267	4.107.472	6.016.774
CREAM 2 % 1 15 G	2.939.575	2.463.935	1.370.418	5.320.856
DEXTROCIN	5.009.244	6.331.854	7.967.170	9.750.556
CREAM 2 % 1 15 G	3.678.372	4.809.047	6.902.379	6.769.786
OINT 2 % 1 15 G	1.330.872	1.522.807	1.064.791	2.980.770
SILVERDIN	6.180.927	8.163.854	9.130.762	9.655.392
CREAM 10 MG 1 40 G	6.045.059	7.930.742	8.956.591	9.410.244
CREAM 10 MG 1 400 G	135.867	233.112	174.171	245.149
THIOCILLINE	3.674.307	4.521.985	4.075.880	5.832.694
OINT 1 30 G	3.674.307	4.521.985	4.075.880	5.832.694
BALABAN	2.436.268	2.031.934	2.176.566	4.502.643
OINT 2 % 1 15 G	2.436.268	2.031.934	2.176.566	4.502.643
STAFINE	1.986.266	2.860.011	3.193.842	3.590.112
CREAM 2 % 1 15 G	1.278.826	1.684.045	1.948.604	2.252.738
OINT 2 % 1 15 G	707.439	1.175.966	1.245.238	1.337.373
FUCITEC	1.400.698	1.892.069	1.966.775	2.563.581
CREAM 2 % 1 20 G	983.238	1.338.419	1.352.491	1.782.993
OINT 2 % 1 20 G	417.461	553.650	614.284	780.588
SILVERDIN PLUS	1.559.151	1.417.664	1.542.803	2.299.436
CREAM 1 50 G	1.559.151	1.417.664	1.542.803	2.299.436
BACTROBAN	4.143.221	3.741.698	7.553.226	2.231.906
OINT 2 % 1 15 G	4.143.221	3.738.242	7.553.260	2.231.906
CREAM 2 % 1 15 G	0	3.456	-33	0
FUSIDAS	403.607	575.731	422.209	469.330
CREAM 2 % 1 20 G	403.607	575.731	422.209	469.330
MUPIDERM	140.487	543.302	314.266	425.146
OINT 2 % 1 15 G	140.487	543.302	314.266	425.146
TIREMIX	240.541	174.241	240.693	394.144
CREAM 2 % 1 20 G	240.541	174.241	240.693	394.144
SILVAMED	244.050	1.464	238.732	301.848
CREAM 1 % 1 40 G	244.050	1.464	238.732	301.848
DERISIV	8.484	8.240	162.826	167.998
CREAM 1 40 G	8.484	8.240	162.826	167.998
FUCIDOX	7.206	0	0	148.162
CREAM 2 % 1 20 G	7.206	0	0	148.162
SILVADIAZIN	59.852	48.695	84.922	76.754
CREAM 400 MG 1 40 G	59.852	48.695	84.922	76.754
		1	1	

POLIMISIN	12.539	3.106	9.721	10.521
OINT 1 14 G	12.539	3.106	9.721	10.521
FUCIBEST	187	22.361	31.838	0
CREAM 2 % 1 20 G	187	22.361	31.838	0
FUSIX DERMA	231.925	0	0	0
CREAM 2 % 1 20 G	90.312	0	0	0
OINT 2 % 1 20 G	141.614	0	0	0

Table 3.4. Topical antibacterials retail sales analysis in units [55]

PRODUCT NAME	TL Year/16	TL Year/17	TL Year/18
TOPICAL ANTIBACTERIALS	11.936.178	13.302.203	13.242.694
FUCIDIN	2.480.255	2.509.169	2.621.604
TERRAMYCIN	1.101.696	2.239.491	1.903.142
BACODERM	1.201.180	884.465	1.401.813
DEXTROCIN	1.054.158	1.118.569	1.159.334
SILVERDIN	2.358.081	2.440.709	2.198.159
THIOCILLINE	1.149.658	926.021	1.145.337
BALABAN	393.874	423.314	735.887
STAFINE	718.682	742.089	702.394
FUCITEC	402.206	395.115	438.454
SILVERDIN PLUS	211.617	208.029	271.669
BACTROBAN	541.701	1.033.865	241.474
FUSIDAS	155.433	103.911	98.522
MUPIDERM	100.954	49.610	53.409
TIREMIX	37.917	49.382	73.614
SILVAMED	907	73.801	79.904
DERISIV	3.560	68.653	71.536
FUCIDOX	0	0	23.032
SILVADIAZIN	17.889	28.270	21.746
POLIMISIN	472	1.607	1.664
FUCIBEST	5.938	6.133	0
FUSIX DERMA	0	0	0

Table 3.5. Antiseptics and disinfectants retail sales value analysis in TL [55]

PRODUCT NAME	TL YTD/6/2019	TL Year/16	TL Year/17	TL Year/18
TOTAL MARKET	17.506.956	27.788.933	32.227.229	32.006.143
<b>BEPANTHENE PLUS</b>	7.261.739	8.701.134	10.330.432	11.953.917

CDEAM 120 C	7 261 720	9 701 124	10 220 422	11.052.017
CREAM 1 30 G	7.261.739	8.701.134	10.330.432	11.953.917
BATTICON	4.876.661	8.124.391	10.230.407	9.928.184
SOLUT. 10 % 1 30 ML	2.479.354	3.946.785	5.148.209	5.065.017
SOLUT. 10 % 1 100 ML	2.397.307	3.924.307	5.071.535	4.863.167
SOLUT. 10 % 1 1000	0	252.540	10.663	0
SOLUT. 10 % 1 250 ML	0	760	0	0
FURACIN	2.877.297	4.256.075	4.657.644	5.448.448
SOL.DRESSING 1 56 G	2.877.297	4.256.075	4.657.644	5.448.448
BIOKADIN	1.421.506	2.429.756	2.623.612	2.438.912
SOLUT. 10 % 1 30 ML	668.819	1.132.135	1.200.281	1.147.588
SOLUT. 10 % 1 100 ML	646.542	1.208.488	1.263.197	1.108.620
SOLUT. 10 % 1 1000	106.145	89.134	160.135	182.705
BATIODIN	578.734	2.479.458	2.823.503	1.596.537
SOLUT. 10 % 1 100 ML	228.405	1.220.786	1.333.551	682.015
SOLUT. 10 % 1 30 ML	183.515	819.879	935.088	516.204
SPRAY 10 % 1 100 ML	73.950	178.161	235.812	162.189
SPRAY 10 % 1 30 ML	81.278	173.924	189.594	147.295
SOLUT. 10 % 1 1000	11.585	86.708	129.458	88.835
BATIKAR	207.540	518.230	480.497	396.293
SOLUT. 10 % 1 100 ML	93.581	268.692	231.183	194.359
SOLUT. 10 % 1 30 ML	89.846	218.349	195.273	160.079
SOLUT. 10 % 1 1000	24.113	31.188	54.041	41.855
BETAKON	24.181	6.654	82.929	90.625
SOLUT. 68 % 1 100 ML	24.181	6.562	82.215	89.590
SOLUT. 10 % 1 1000	0	92	713	1.035
RIVANOL	94.532	39.270	82.329	68.029
POWD. 1 G 25	52.332	39.270	81.805	51.851
POWD. SACHET 1 G 25	42.200	0	524	16.178
NITROCIN	20.091	0	35.985	41.692
OINT .20 % 1 56 G	20.091	0	35.985	41.692
DERMATOL	173	195	529	26.327
POWD. 1 5 G	173	195	529	26.327
DEXPANTEN PLUS	113.013	0	28.298	8.726
CREAM 1 30 G	113.013	0	28.298	8.726
PERMASOL	37	1.214.868	827.599	4.521
TABS SOLUB 250 MG	37	1.214.868	827.599	4.521
FARMAZOL	0	16.700	22.721	2.332
SOLUT. 1 500 ML	0	16.700	22.721	2.332
FURADERM	31.404	15	6	1.468
OINT .20 % 1 56 G	31.404	15	6	1.468
POVIIODEKS	49	0	98	99
SOLUT. 10 % 1 100 ML	4	0	63	79
56161.10 /01100 MIL	<b>T</b>	U	05	17

SOLUT. 10 % 1 30 ML	45	0	7	17
SOLUT. 10 % 1 1000	0	0	29	4
BATOL	0	1.000	587	14
SOLUT. 10 % 1 20 ML	0	262	129	7
SPRAY 10 % 1 100 ML	0	524	320	7
SOLUT. 10 % 1 50 ML	0	214	138	0
ZEFIROLUM	0	0	0	14
SOLUT. 1 1000 ML	0	0	0	14
ISOSOL	0	293	46	7
SOLUT. 10 % 1 100 ML	0	293	46	7
ALCOHOL. SOL 10 %	0	0	0	0
OINT 10 % 1 20 G	0	0	0	0
OINT 10 % 1 70 G	0	0	0	0
OINT 10 % 5 1 G	0	0	0	0
SOLUT. 1 250 ML	0	0	0	0
SOLUT. 10 % 1 1000	0	0	0	0
SOLUT. 10 % 1 50 ML	0	0	0	0
SOLUT. 10 % 1 500 ML	0	0	0	0
DETTOL	0	55	0	0
SPRAY 1 100 ML	0	55	0	0
EGZA	0	0	1	0
SOAP 1 100 ML	0	0	1	0
KLORHEKSOL	0	0	0	0
FOAM 1 200 ML	0	0	0	0
KLORHEX	0	789	0	0
SOLUT. 4 % 1 1000 ML	0	789	0	0
MERKROMOL	0	0	0	0
SOLUT. 2 % 1 20 ML	0	0	0	0
SOLUT. 2 % 1 50 ML	0	0	0	0
MERSOL	0	0	0	0
SOLUT. 2 % 1 50 ML	0	0	0	0
PANTENOL PLUS	0	0	0	0
CREAM 1 30 G	0	0	0	0
POLIVIDON	0	0	0	0
SOLUT. 10 % 1 100 ML	0	0	0	0
SOLUT. 10 % 1 30 ML	0	0	0	0
POLYOD	0	0	6	0
SOLUT. 10 % 1 100 ML	0	0	6	0
SAVLEX	0	0	0	0
SOLUT. 1 100 ML	0	0	0	0
SAVONOL	0	0	0	0
SOLUT. 1 100 ML	0	0	0	0

PRODUCT NAME	Units Year/16	Units Year/17	Units Year/18
BATTICON	1.310.488	1.506.603	1.281.796
FURACIN	1.916.738	1.883.862	1.902.824
BIOKADIN	456.870	395.431	315.282
BATIODIN	535.693	484.926	236.970
BATIKAR	190.631	184.899	154.004
BETAKON	2.160	22.302	21.143
RIVANOL	23.903	35.337	18.412
NITROCIN	0	15.408	16.131
DERMATOL	651	1.724	5.920
DEXPANTEN PLUS	0	7.077	2.338
PERMASOL	82.981	44.677	218
FARMAZOL	2.778	2.798	284
FURADERM	6	2	486
POVIIODEKS	0	458	344
BATOL	282	155	3
ZEFIROLUM	0	0	8
ISOSOL	45	7	1
DETTOL	10	173	0
EGZA	0	10	0
KLORHEKSOL	0	0	0
KLORHEX	38	0	0
MERKROMOL	0	0	0
MERSOL	0	0	0
PANTENOL PLUS	0	0	0
POLIVIDON	0	0	0
POLYOD	75	36	0
SAVLEX	0	0	0
SAVONOL	0	0	0
ZEFIRAN	5	0	0
POLYOD	75	36	0
SAVLEX	0	0	0
ZEFIRAN	5	0	0
ZEFORT	222	20	0
ZEFIRAN	5	0	0
ZEFORT	222	20	0

Table 3.6. Antiseptics and disinfectants retail sales value analysis in units [55]

PRODUCT NAME	TL YTD/6/2019	TL Year/16	TL Year/17	TL Year/18
TOTAL MARKET	70.561.635	55.277.423	78.177.832	97.692.546
HAMETAN	20.539.580	23.910.502	25.803.373	31.580.283
OINT 25 % 1 30 G	10.485.546	11.850.904	13.359.871	16.261.517
CREAM 5.35 % 1 30 G	10.054.034	12.059.597	12.443.502	15.318.766
MADECASSOL	25.379.221	10.355.758	22.306.419	30.644.754
OINT 40 MG 1 40 G	25.379.221	10.355.758	22.306.419	30.644.754
FITO	17.452.087	16.646.733	22.044.964	25.425.210
CREAM 1 40 G	17.452.087	16.646.733	22.044.964	25.425.210
HAMAZINC	4.001.564	1.175.621	4.736.194	6.071.899
CREAM 1 30 G	4.001.564	527.289	4.729.005	6.071.887
CREAM 1 60 G	0	648.332	7.189	12
GARMASTAN	1.809.729	2.935.376	3.144.432	3.567.702
OINT .05 % 1 20 G	1.809.729	2.935.376	3.144.432	3.567.702
MADEGCENTA	371.326	0	0	160.094
OINT 1 % 1 40 G	371.326	0	0	160.094
DEXPANTEN	168.698	139.247	72.254	151.055
OINT 5 % 1 30 G	114.655	61.783	46.810	78.784
CREAM 5 % 1 30 G	54.043	77.464	25.444	72.271
PANTENOL	35.912	91.764	36.131	76.206
OINT 5 % 1 30 G	27.680	71.235	32.082	61.536
CREAM 5 % 1 30 G	8.232	20.529	4.049	14.670
ARMATHENE	0	22.421	34.066	15.341
CREAM 5 % 1 30 G	0	22.421	34.066	15.341
BEPANTHENE	0	0	0	0
CREAM 5 % 1 100 G	0	0	0	0
CREAM 5 % 1 30 G	0	0	0	0
OINT 5 % 1 100 G	0	0	0	0
OINT 5 % 1 30 G	0	0	0	0
MADEFIX	803.519	0	0	0
OINT 1 % 1 40 G	803.519	0	0	0
NOVUXOL	0	0	0	0
OINT 1.20 IU 1 30 G	0	0	0	0

Table 3.7. Other wound healing agents retail sales value analysis in TL [55]

Table 3.8. Other wound healing agents retail sales value analysis in units [55]

PRODUCT NAME	Units	Units	Units
	Year/16	Year/17	Year/18
TOTAL MARKET	10.650.018	12.361.160	13.328.452

HAMETAN	5.756.301	6.055.866	6.275.368
MADECASSOL	1.946.777	2.095.373	2.508.772
FITO	2.547.219	2.926.024	2.911.321
HAMAZINC	206.083	1.144.892	1.445.313
GARMASTAN	109.331	95.411	89.689
MADEGCENTA	0	0	14.043
DEXPANTEN	38.333	24.290	57.626
PANTENOL	36.073	12.567	23.214
ARMATHENE	9.901	6.737	3.106
BEPANTHENE	0	0	0
MADEFIX	0	0	0
NOVUXOL	0	0	0

Table 3.9. Other dermatological preperation retail sales value analysis in TL [55]

PRODUCT NAME	TL	TL	TL	TL
	YTD/6/2019	Year/16	Year/17	Year/18
TOTAL MARKET	23.297.459	28.429.993	32.511.003	38.532.942
CONTRACTUBEX	7.980.712	11.848.589	13.069.709	14.298.906
GEL 1 120 G	7.980.712	11.848.617	13.069.681	14.298.821
GEL 1 100 G	0	-28	28	85
EXPIGMENT	3.098.832	3.265.697	3.810.050	5.137.120
CREAM 4 % 1 30 G	2.309.472	2.353.232	2.800.973	3.857.244
CREAM 2 % 1 30 G	789.361	912.466	1.009.077	1.279.876
VERRUTOL	2.996.426	3.542.180	4.007.851	5.032.865
SOLUT. 1 15 G	2.996.426	3.542.180	4.007.851	5.032.865
URESAL	2.109.985	2.667.358	3.154.800	3.506.023
OINT FORT 1 50 G	2.109.985	2.667.358	3.154.800	3.506.023
PROPECIA	2.653.414	3.524.862	3.468.835	3.444.443
FILMTAB 1 MG 28	2.653.414	3.524.862	3.468.835	3.444.443
DUODERM	1.779.433	2.216.577	2.488.145	2.882.982
SOLUT. 1 15 G	1.779.433	2.216.577	2.488.145	2.882.982
NOSKAR	1.298.139	0	820.572	1.980.707
GEL 1 100 G	1.298.139	0	820.572	1.980.707
IL 33	413.204	652.266	672.230	821.070
SOLUT. 1 10 ML	413.204	652.266	672.230	821.070
BIOAK	589.876	138.454	390.908	678.242
TABS 5 MG 30	589.876	138.454	390.908	678.242
VITIX	176.106	569.911	528.857	486.359
TABS 30	176.106	569.911	528.857	486.359
HIOTIN	187.333	1.244	99.045	245.530
TABS 5 MG 30	187.333	1.244	99.045	245.530

HEPATUBEX	13.999	0	0	18.694
GEL 1 120 G	13.999	0	0	18.694
ARK STING. NETTLE	0	0	0	0
CAPS 45	0	0	0	0
DILAN	0	64	0	0
SOLUT. 1 20 ML	0	64	0	0
THOMPS. MANGOSTEEN	0	0	0	0
CAPS 475 MG 30	0	0	0	0
WARTNER	0	2.790	0	0
FOOT AERO 1 50 ML	0	0	0	0
HAND AERO 1 50 ML	0	2.790	0	0

Table 3.10. Other dermatological preperation retail sales analysis in units [55]

PRODUCT NAME	Units Year/16	Units Year/17	Units Year/18
CONTRACTUBEX	213.391	215.573	206.441
EXPIGMENT	651.202	686.329	796.221
VERRUTOL	487.025	502.869	544.827
URESAL	543.958	581.100	556.700
PROPECIA	43.728	39.328	34.007
DUODERM	450.189	461.249	462.681
NOSKAR	0	38.175	76.118
IL 33	52.717	44.014	46.986
BIOAK	20.058	52.737	76.889
VITIX	4.676	3.913	2.974
HIOTIN	183	13.569	28.905
HEPATUBEX	0	0	371
ARK STING. NETTLE	0	0	0
DILAN	10	0	0
THOMPS. MANGOSTEEN	0	0	0
WARTNER	112	0	0
ANTISEPTICS+DISINFECTANTS	5.627.093	5.754.386	5.135.781
BEPANTHENE PLUS	1.103.739	1.168.501	1.179.617

Table 3.11. Retail and hospital wound healing sales value analysis in TL [55]

	TL	TL	TL
MARKET	<b>Retail+Hospital</b>	<b>Retail+Hospital</b>	<b>Retail+Hospital</b>
	Year/16	Year/17	Year/18
TOTAL	181.526.462	229.739.327	270.661.659

OTH WOUND HEALING			
AGENTS	58.158.884	82.009.244	103.178.126
HAMETAN	25.026.373	27.204.370	33.577.640
MADECASSOL	10.460.165	22.526.133	30.981.099
FITO	18.094.930	24.023.699	28.302.920
HAMAZINC	1.177.278	4.754.381	6.125.538
GARMASTAN	2.996.622	3.255.760	3.686.234
DEXPANTEN	142.462	72.465	191.994
MADEGCENTA	0	0	161.303
PANTENOL	238.108	138.371	130.165
ARMATHENE	22.421	34.066	21.232
BEPANTHENE	54	0	0
GELFIX	472	0	0
MADEFIX	0	0	0
NOVUXOL	0	0	0
TOPICAL			04 17 ( 000
ANTIBACTERIALS	64.486.592	79.791.778	94.176.882
FUCIDIN	13.935.222	16.717.561	21.483.296
TERRAMYCIN	8.132.124	15.456.803	15.341.040
BACODERM	7.096.070	5.486.767	11.352.772
SILVERDIN	9.237.207	10.294.306	10.525.082
DEXTROCIN	6.436.118	8.086.561	9.940.271
THIOCILLINE	5.354.903	5.009.453	7.177.128
BALABAN	2.658.607	2.590.389	5.341.711
STAFINE	2.887.862	3.222.557	3.607.126
FUCITEC	1.922.446	1.983.892	2.574.352
SILVERDIN PLUS	1.419.072	1.543.170	2.299.670
BACTROBAN	3.812.962	7.611.049	2.236.580
MUPIDERM	653.626	441.644	559.990
FUSIDAS	576.070	437.814	526.101
TIREMIX	175.316	249.871	421.541
SILVAMED	71.354	278.588	322.017
DERISIV	31.817	240.544	210.648
FUCIDOX	0	0	148.615
SILVADIAZIN	51.072	85.354	95.672
POLIMISIN	3.121	23.528	13.272
FUCIBEST	31.626	31.928	0
FUSIX DERMA	0	0	0
OTHER			
DERMATOLOGICAL	28.446.258	32.529.491	38.553.296
PREP			
CONTRACTUBEX	11.860.364	13.082.779	14.314.644
EXPIGMENT	3.265.950	3.810.141	5.137.419
VERRUTOL	3.542.422	4.008.172	5.032.990

2.669.988	3.157.624	3.509.060
3.525.183	3.470.451	3.444.174
2.216.685	2.488.295	2.883.065
0	820.604	1.980.890
652.593	672.435	821.533
138.454	390.953	678.580
570.515	528.857	486.359
1.251	99.180	245.888
0	0	18.694
0	0	0
64	0	0
0	0	0
0	0	0
2.790	0	0
30 434 728	35 408 813	34.753.355
50.454.720	35.400.015	54.755.555
8.914.809	10.608.596	12.216.352
8.125.635	10.231.421	9.929.879
6.333.434	7.189.582	7.329.795
2.459.164	2.653.201	2.465.673
2.483.586	2.827.478	1.597.218
518.230	480.514	396.293
254.481	224.912	319.462
0	54.270	202.783
7.118	88.744	95.647
39.342	82.951	68.189
55.867	76.848	55.898
0	28.298	28.081
195	529	26.327
0	4.519	10.333
1.215.958	828.274	4.521
0	878	2.692
16.700	22.721	2.332
523	6	1.468
3.317	2.042	384
1.000	587	14
0		14
55	0	0
0	1	0
		0
		0
		0
0	0	0
	$\begin{array}{r} 3.525.183\\ 2.216.685\\ 0\\ 0\\ 652.593\\ 138.454\\ 570.515\\ 1.251\\ 0\\ 0\\ 0\\ 64\\ 0\\ 2.790\\ 30.434.728\\ 8.914.809\\ 8.125.635\\ 6.333.434\\ 2.459.164\\ 2.483.586\\ 518.230\\ 254.481\\ 0\\ 7.118\\ 39.342\\ 55.867\\ 0\\ 1.215.958\\ 0\\ 1.215.958\\ 0\\ 1.215.958\\ 0\\ 1.215.958\\ 0\\ 1.215.958\\ 0\\ 1.215.958\\ 0\\ 1.215.958\\ 0\\ 1.215.958\\ 0\\ 1.215.958\\ 0\\ 1.215.958\\ 0\\ 1.215.958\\ 0\\ 1.215.958\\ 0\\ 1.215.958\\ 0\\ 0\\ 1.215.958\\ 0\\ 0\\ 1.215.958\\ 0\\ 0\\ 1.215.958\\ 0\\ 0\\ 1.215.958\\ 0\\ 0\\ 1.215.958\\ 0\\ 0\\ 1.215.958\\ 0\\ 0\\ 1.215.958\\ 0\\ 0\\ 1.215.958\\ 0\\ 0\\ 1.215.958\\ 0\\ 0\\ 1.215.958\\ 0\\ 0\\ 1.215.958\\ 0\\ 0\\ 1.215.958\\ 0\\ 0\\ 1.215.958\\ 0\\ 0\\ 1.215.958\\ 0\\ 0\\ 0\\ 1.215.958\\ 0\\ 0\\ 0\\ 0\\ 0\\ 0\\ 0\\ 0\\ 0\\ 0\\ 0\\ 0\\ 0\\$	$\begin{array}{c cccccc} 3.525.183 & 3.470.451 \\ \hline 2.216.685 & 2.488.295 \\ \hline 0 & 820.604 \\ \hline 652.593 & 672.435 \\ \hline 138.454 & 390.953 \\ \hline 570.515 & 528.857 \\ \hline 1.251 & 99.180 \\ \hline 0 & 0 \\ \hline 1 \\ \hline 0 & 0 \\ \hline 0 \\ \hline 0 & 0 \\ \hline 0 \\ \hline 0 & 0 \\ \hline 0 \\ \hline 0 & 0 \\ \hline 0 \\ \hline 0 & 0 \\ \hline$

POLYOD	0	6	0
SAVLEX	0	0	0
ZEFIRAN	50	0	0
ZEFORT	1.067	96	0
ZEFIRAN	50	0	0
ZEFORT	1.067	96	0

Table 3.12. World sales analysis of the related market in Euro [55]

PRODUCT NAME	Euro	Euro	Euro	Euro
I KODUCI MAME	Year/15	Year/16	Year/17	Year/18
SANTYL	278.884.974	296.395.926	298.644.098	291.427.428
MUPIROCIN GLMK	33.051.759	123.523.589	137.174.021	136.777.036
CHLORAPREP	114.331.150	112.078.343	105.374.107	125.782.982
SURGICEL	118.789.967	125.511.710	123.534.932	118.524.697
BEPANTHEN	89.569.249	98.155.725	105.084.438	109.530.538
C.P.JASPER	138.555.978	137.922.616	104.214.404	96.560.698
FUCIDIN	72.273.460	78.019.662	78.940.681	81.547.418
BETAISODONA	53.219.012	57.831.941	57.438.438	59.534.632
ABREVA	64.206.118	57.052.895	58.780.110	58.709.619
BETADINE	51.423.791	54.515.073	54.200.559	56.288.009
DENAVIR	61.275.506	60.527.275	53.378.424	43.783.849
ZOVIRAX	38.305.830	39.256.895	39.142.745	41.399.138
OCTENISEPT	33.951.034	37.235.322	38.205.651	41.068.028
MIRAMISTIN INFD	21.624.852	28.465.748	32.974.232	35.005.587
BACTROBAN	58.958.651	25.832.190	41.237.720	29.955.261
SURGIFOAM	24.824.929	26.665.311	22.740.595	28.700.351
NEOSPORIN	33.458.538	27.797.101	25.606.058	27.316.042
PAPAW	19.356.001	17.869.929	22.078.405	26.001.255
ACICLOVIR MYLA	75.888.612	62.027.391	34.806.208	24.557.229
GELFOAM	37.995.740	36.878.088	36.353.715	24.099.638
MEBO	24.613.186	29.950.301	23.923.221	23.751.068
FIBLAST	25.959.795	26.223.329	26.116.191	23.264.079
YOU KE SHI	18.652.303	23.232.482	23.734.230	23.217.267
FU NUO	11.388.206	15.356.481	19.516.099	22.913.826
DETTOL	16.457.167	19.587.628	21.516.722	21.905.729
MUPIROCIN TARP	16.932.248	19.236.424	18.771.769	21.685.220
BEPANTHEN PLUS	18.185.750	19.103.603	20.184.533	20.079.849
GENTAMICIN PERR	18.411.751	24.271.018	24.591.582	18.209.018
DERMAGLOS	7.090.975	10.550.823	14.369.582	17.612.994
METRONIDAZOLE TARP	23.854.994	29.719.913	20.125.039	17.221.168

#### 3.2. PRESCRIPTION ANALYSIS OF WOUND HEAILING PRODUCTS

IQVIA's prescription information are used to measure market and product demand. The prescription information are collected by the physicians to have broader insight about the market. Dermobor market were analyzed in Table 3.13-16 based on the physicians'speciality.

Year/18	Number of Prescription
WOUND HEALING AGENTS	2.630.564
DERM	1.104.688
PAED.	981.917
SURG.	266.703
GYN	107.832
OTORH	84.969
OTHER	84.454

Table 3.13. Wound healing agents prescription market data vs. specialities [55]

Table 3.14. Topical antibacterials prescription market data vs. specialities [55]

Year/18	Number of Prescription	
TOPICAL ANTIBACTERIALS	2.209.646	
DERM	860.437	
SURG.	485.919	
PAED.	349.484	
OTORH	147.380	
OTHER	366.426	

Table 3.15. Other dermatological prep prescription market data vs. specialities [55]

Year/18	Number of Prescription	
DERMATOLOGICAL PREP	584.220	
DERM	474.519	
GYN	52.241	
SURG.	28.224	
OTHER	29.236	

Year/18	Number of Prescription	
ANTISEPTICS+DISINFECTANTS	583.650	
SURG.	259.012	
PAED.	147.206	
DERM	50.956	
GYN	44.475	
OTHER	82.001	

Table 3.16. Antiseptics and disinfectants market prescription data vs. specialities [55]

#### 3.3. STAKEHOLDER ANALYSIS OF WOUND HEALING PRODUCTS

Some hospitals in Turkey set up their own wound care clinics and committee. Wound care council has members interdisiplinarty including, vascular surgery, orthopedics, endocrinology/diabetes, infectious diseases, hyperbaric medicine, plastic surgery, dermatology, physiotherapy and general surgery. also other associations that are vascular surgery, diabetes, general surgery, trauma and infectious diseases society have also specific wound care sessions in their congress.

Table 3.17. Wound and Diabetic Foot Council unit in Turkey

Hospitals Name	City
Umraniye Hospital	Istanbul
Haydarpasa Numune TRH	Istanbul
Dr. Lutfi Kırdar TRH	Istanbul
Medeniyet University	Istanbul
Sultan Abdülhamid Han TRH	Istanbul
Sehir Prof. Dr.İlhan Varank TRH	Istanbul
Fatih Sultan Mehmet TRH	Istanbul
Gulhane TRH	Ankara
Diskapi Yildirim Beyazit TRH	Ankara
Ankara Fizik Tedavi and Rehebilitasyon	Ankara
Gaziler Fizik Tedavi and Rehabilitasyon	Ankara
Yunus Emre State Hospital	Eskisehir
Sakarya University	Sakarya
Yuksek Ihtisas	Bursa
Bozyaka TRH	Izmir
Necip Fazil Sehir Hospital	K.Maras
Iskendurun State Hospital	Hatay
Dr. Ersin Arslan Hospital	G. Antep
Mehmet Akif Inan TRH	S. Urfa

Turkish Wound Management Society organized their congress and nurse training course annouly.

Key Opinion Leader Name	Responsibilitiy	
Ayişe Karadağ	President of the Wound Care Association	
Ali Barutcu	Associate President of the Wound Care Association	
Neșe Saltoğlu	Member of the Diabetic Foot Infection Working Group	
Bülent Ertugrul	President of the Diabetic Foot Infection Working Group	
Ozge Turan		
Nese Saltoglu		
Ayten Kadanalı		
Aynur Engin	Member of the Diabetic Foot Infection Working Group	
Oznur Ak		
Alper Sener		

Table 3.18. Key opinion leader in Turkey

### 3.4. CONSUMER BEHAVIOUR ANALYSIS

An online survey conducted to understand consumer behaviour about the frequently used dermatological products for the burn wound care, wound healing and herpes simplex respectively. Four questions were answered by 381 respondents. Table 3.19, 3.20 and 3.21 shows the number of the preferred brands for the indications that has been questioned. Table 3.22 indicates the ratio that the decision of the respondents affected by a tripple effect of a dermatological brand.

Table 3.19.	First chosen	brand of	consumer	for	burn wou	nd
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Burn Wound Care Brands	Percentage Preference	Number of Respondents
Hametan	8.70%	32
Silverdin	66.58%	245
Furacin	0.27%	1
Madecassol	5.71%	21
Bepanthene	15.49%	57
Terramycin	3.26%	12

Wound Healing Brands	Percentage Preference	Number of Respondents
Furacin	6.09%	21
Madecassol	34.78%	120
Thiocilline	3.77%	13
Contructubex	18.55%	64
Fucidin	15.65%	54
Bactroban	21.16%	73

Table 3.20. First chosen brand of consumer for wound healing

Table 3.21. First chosen brand of consumer for Herpes Simplex

Herpes Simplex Brands	Percentage Preference	Number of Respondents
Terramycin	18.05%	63
Zovirax	61.03%	213
Vectavir	18.05%	63
Dermo-Trosyd	2.87%	10

## Table 3.22. Comments on triple effect for a brand

Triple Effect affected the decision to select a brand	Percentage Preference	Number of Respondents
Completely Non-Agreed	9.04%	34
Non-Agreed	17.29%	65
Neutral	14.10%	53
Agreed	31.65%	119
Completely Agreed	27.93%	106

## 4. DISCUSSION

The treatment of large and chronic wounds is a big burden to healthcare systems around the world. Chronic wounds affect patients' physical, mental, and social well-being to the same extent as heart and kidney diseases. Management of a patient with a chronic wound requires close cooperation of physicians and other health care workers from related departments. Dermatologists, surgeons, internists, and geriatricians are becoming increasingly involved in the field of wound care. Additionally, general practitioners, family physicians and even the pharmacists are frequently required to have broad knowledge about the treatment of acute and chronic wounds.

The known diabeties patients number is seven million in Turkey. According to the MEDULA registry of Turkey, approximately 5 million of those patients have also diabetes foot wound and near 500.000 of it has infection additionally. On the other hand, it is estimated that annually 308,796 patients in Turkey are likely to develop pressure sore with a cost of 1 billion 425 million US Dollars.

According to the IQVIA data, the wound healing market value costs 270 million Turkish Lira regarding 37 million unit sales including retail and hospital market data. On the other hand, the reatil wound healing market values is 258 million Turkish Lira. The percentage of hospital market is 4,6% in value. Hence, it can be understood that the gaining brand awareness in retail market is more critical than hospital market. However, the data is not shown wich product is more preffered in hospital market [55].

According to the 34 Countries World Data of IQVIA, the wound healing market is 3,5 billion Euro. The most preferred three product is Santyl (colloganese), Mupirocin (Mupirocin) and Chloraprep (Chlorhexidine Gluconate). Active ingredients of Santly and Chloraprep not found in Turkey. Dermabor Gel includes 0.2 percent Chlorhexidine Digluconate. Products which includes Chlorhexidine Digluconate uses in Turkey mainly for the mouthwash. Only Coresatin has been positioned for wound healing.

As a current treatment, doctors and nurses help the wound along with a variety of dressings, antibiotics to prevent infection, and medical debridement, which removes unhealthy tissue to stimulate regrowth. Each expenditure item for chronic wound management in Turkey has been indicated in Table 1.4.

Mildly infected wounds probably require topical antibiotics. All severe and some moderate infections should at least be initially treated with intravenous antibiotics. Duration of therapy also depends on severity. Treatment for 1 to 2 weeks may be sufficient for mild infections, while moderate and severe should be treated for 2 to 4 weeks. Length of treatment also depends on effectiveness of concomitant therapy. According to the reserach that is written Gencer ZE and et all., one patient with a pressure ulcer approximately bring 15.000 TL economic burden. Approximatly 25 percent of it comes from antibiotics [38].

Antibacterials and wound healing market is 3 times bigger than the antiseptic and disinfectants and other dermatological preparation. The first ranked product in terms of value in the topical antibacterilas market is Fucidin. Thiocilline, Silverdin, Bacoderm are the other valuable brand in this market. On the other hand, the most valuable product in the wound healing market is Hametan, Madecassol and Fito Cream. According to the consumer analysis, the first wound healing product is Madecassol. Controtubex which belongs to the other preparation class according to the ATC classification has also high preferance rate. As the Cantratubex is well-known and positioned as a scar removal gel in the market, it shows that consumer considered significantly the scar removel when they think wound healing. The other product Madecasol is famous with its cell regeneration. Removal of scar and cell regeration claims are really effective on the consumer. Consurmers prefer Hametan at most for the burn wound. It is written similar indication in all those product prescription but they differentiate more for one of the indication. Some brands differentiate themselves with the help of the form variation like Bepanthen case.

### 5. CONCLUSION

Dermobor has the power owning the wound care market started with the chronic wound treatment and hence the chronic market recognition of the brand will lead to becoming stronger Dermobor gradually on acute market. Dermobor is a product against virus, bacteria, fungal disease and yeast. Dermobor allows physiological debridement without needing any instruments and chemical substances. It is not only antiseptic gel but also is effective a wound healing products. It shortens the treamenet duration with using 3 times in a day. Early phase usage of Dermobor prevents the wound to be severe chronic wound. Costs can be significantly reduced while improving wound care management and infection control. It is really critical to avoid infection in the acute phase in order not to become the wound chronic and infected. Uninfected ulcer and acute wound commonly treated with the product with pharmacist's advice. Pharmacists should have experience about the treatment of infection for the patients that have chronic wounds. They should refer patients to physicians in case lack of progression of healing and increased severity of the wound. Development of preventive activities, raising awareness among the healthcare staff, and early detection of the cases will substantially reduce the financial loss arising from chronic wound. In Turkey, there are lots of resources to provide online education to the wound care council however it is missing a big portal sponsored by a company to own the indication in terms of the product portfolio and creating value. To spread the experience with the product usage among clinicans could be written more product evoluation researh with volunteer key opinion leader. Product evoluation research could increase the believe of clinically effectiveness and cost effectiveness whilst giving feedback/comments from clinicians, highlighting some of the uses in case studies.

#### REFERENCES

- 1. Rosenbaum AJ1, Banerjee S, Rezak KM, Uhl RL. Advances in wound management. *Journal of the American Academy of Orthopaedic Surgeons*. 2018;26(23):833-843.
- 2. Lindholm C, Searle R. Wound management for the 21st century: Combining effectiveness and efficiency. *International Wound Journal*. 2016;13(2):5-15.
- Wang PH, Huang BS, Horng HC, Yeh CC, Chen YJ. Wound healing. *Journal of Chinese Medical Association*. 2018;81(2):94-101.
- HSE National Wound Management Guidelines 2018 [cited 2018 14 September] Available from: http://www.hse.ie/eng/about/who/onmsd.
- Woo YC, Park SS, Subieta AR, Brennan TJ. Changes in tissue pH and temperature after incision indicate acidosis may contribute to postoperative pain. *Anesthesiology*. 2004; 101:468–475.
- 6. Falanga V. Wound healing and its impairment in the diabetic foot. *Lancet*. 2005;366:1736–1743.
- 7. Schultz GS, Sibbald RG, Falanga V. et al. Wound bed preparation: a systematic approach to wound management. *Wound Repair Regen.* 2003;11(1):1–28.
- 8. McCarty SM, Percival SL. Proteases and delayed wound healing. *Advances in Wound Care*. 2013;2:438–447.
- 9. Schreml S, Szeimies RM, Prantl L, Karrer S, Landthaler M, Babilas P. Oxygen in acute and chronic wound healing. *The British Journal of Dermatology*. 2010;163:257–268.
- Dhall S, Do DC, Garcia M, et al. Generating and reversing chronic wounds in diabetic mice by manipulating wound redox parameters. *Journal of Diabetes Research*. 2014;1155(10):562-625.
- Stanley A, Osler T. Senescence and the healing rates of venous ulcers. *Journal of Vascular Surgery*. 2001;33:1206–1211.

- Lobmann R, Ambrosch A, Schultz G, Waldmann K, Schiweck S, Lehnert H. Expression of matrixmetalloproteinases and their inhibitors in the wounds of diabetic and nondiabetic patients. *Diabetologia*. 2002;45:1011–1016.
- Tsourdi E, Barthel A, Rietzsch H, Reichel A, Bornstein SR. Current aspects in the pathophysiology and treatment of chronic wounds in diabetes mellitus. *BioMed Research International*. 2013;1155(10):385-641.
- Bourguignon LY. Matrix hyaluronan-activated CD44 signaling promotes keratinocyte activities and improves abnormal epidermal functions. *American Journal Of Pathology* 2014;184:1912–1919.
- Cook H, Davies KJ, Harding KG, Thomas DW. Defective extracellular matrix reorganization by chronic wound fibroblasts is associated with alterations in TIMP-1, TIMP-2, and MMP-2 activity. *Journal of Investigative* Dermatology. 2000;115:225– 233.
- Telgenhoff D, Shroot B. Cellular senescence mechanisms in chronic wound healing. Cell Death and Differentiation. 2005;12:695–698.
- Wall IB, Moseley R, Baird DM, et al. Fibroblast dysfunction is a key factor in the nonhealing of chronic venous leg ulcers. *Journal of Investigative Dermatology*. 2008;128:2526–2540.
- Bitar MS. The GSK-3beta/Fyn/Nrf2 pathway in fibroblasts and wounds of type 2 diabetes: on the road to an evidence-based therapy of nonhealing wounds. *Adipocyte* 2012;1:161–163.
- Ayello EA, Dowsett C, Schultz GS, Cwon F, Caroline R, Gregory SF. Time heals all wounds. *Nursing*. 2004;34(4):36-42.
- Ministry of Health and Turkish Diabetes Foundation. Diabetes 2020: Vision and Targets-Turkey Final Report. Ankara, Turkey: Turkish Diabetes Foundation, 2010: 57-60.
- Frank W, Mayer T, Hans-Oliver R. Chronic wound care. *The Lancet*. 2008; 372(9653):1860-2.

- 22. Mehraj M. A review of Wagner classification and current concepts in management of diabetic foot. *International Journal of Orthopaedics Sciences*. 2018;4(1):933-935.
- Sherman J. Diabetic foot ulcer assessment and treatment: A pharmacist's guide. US Pharmacits. 2010;35(6):38-44.
- Braun LR, Fisk WA, Lev-Tov H, Kirsner RS, Isseroff RR. Diabetic foot ulcer: an evidence-based treatment update. *American Journal of Clinical Dermatology*. 2014; 15(3):267–281.
- Wound Healing Society's Chronic Wound Care Guidelines 2016 [cited 2019 9 August]. Available from: http://multimedia.3m.com/mws/media/618708O/chronic-wound-careguidelines.pdf.
- Shojaiefard A, Khorgami Z, Larijani B. Independent risk factors for amputation in diabetic foot. *International Journal of Diabetes in Developing Countries*. 2008;28(2):3237.
- 27. Yesil S, Akinci B, Yener S, et al. Predictors of amputation in diabetics with foot ulcer: single center experience in a large Turkish cohort. *Horm (Athens)*. 2009;8(4):286e295.
- 28. Frykberg RG, Zgonis T, Armstrong DG, et al. Diabetic foot disorders. A clinical practice guideline. *The Journal of Foot & Ankle Surgery*. 2006;45(5):1-66.
- Fortington LV, Geertzen JH, van Netten JJ, Postema K, Rommers GM, Dijkstra PU. Short and long term mortality rates after a lower limb amputation. *European Journal* of *Vascular* and *Endovascular Surgery*. 2013;46(1):124e131.
- Won SH, Chung CY, Park MS, et al. Risk factors associated with amputation-free survival in patient with diabetic foot ulcers. *Yonsei Medical Journal*. 2014;55(5): 13731378.
- 31. Singh N, Armstrong DG, Lipsky BA. Preventing foot ulcers in patients with diabetes. *Journal of the American Medical Association*. 2005;293(2):217228.
- 32. İnan DG, Öztunç G. Pressure ulcer prevalence in Turkey: A sample from a university hospital. *Journal of Wound, Ostomy and Continence Nursing*. 2012;39(4):409-413.

- 33. Rice DP. Cost-of-illness studies: fact or fiction? Lancet. 1994;344(8936):1519-20.
- Rice DP, Cost of illness studies: what is good about them? *Journal of Injury Prevention*. 2000;6(3):177–179.
- 35. Russell LB, Siegel JE, Daniels N, Gold MR, Luce BR, Mandelblatt JS. Costeffectiveness analysis as a Guide to resource allocation in Health: roles and limitations. *Cost-effectiveness in Health and Medicine*. 1996:3-24.
- 36. Luce BR, Manning WG, Lipscomb J. Estimating costs in Cost-effectiveness analysis. *Cost-effectiveness in Health and Medicine*. 1996:176-213.
- Gencer ZE, Unal E, Ozkan O. The cost analysis of pressure ulcer treatment; the treatment cost comparison of conventional and modern wound care. *Akdeniz Medical Journal.* 2019; 5(2):201-208.
- Hunt CD. The biochemical effects of physiologic amount of dietary boron in animal nutrition models. *Environmental Health Perspectives*. 1994;102:35–43.
- Hunt CD, Idso JP. Dietary boron as a physiological regulator of normal inflammatory response: a review and current research progress. *Journal of Trace Elements in Medicine and Biology*. 1999;12:221–233.
- Garcia-Gonzalez M, Mateo P, Bonilla I. Boron requirement for envelope structure and function in Anabaena PCC 7119 heterocysts. *Journal of Experimental Botany*. 1991;42:925–929.
- Benderdour M, Van Bui T, Hess K, et al. Effects of boron derivatives on extracellular matrix formation. *Journal of Trace Elements in Medicine and Biology*. 2000;14:168– 173.
- 42. Chebassier N, El Houssein O, Viegas I, et al. In vitro induction of matrix metalloproteinase2 and matrix metalloproteinase-9 expression in keratinocytes by boron and manganese. *Experimental Dermatology*. 2004;13:484–490.
- Nzietchueng RM, Dousset B, Franck P, et al. Mechanisms implicated in the effects of boron on wound healing. *Journal of Trace Elements in Medicine and Biology*. 2002;16:239–244.

- 44. Heilmann S, Küchler S, Wischke C, Lendlein A, Stein C, Schäfer-Korting M. A thermosensitive morphine-containing hydrogel for the treatment of large-scale skin wounds. *International Journal of Pharmaceutics*. 2013;444(1):96–102.
- 45. Kant V, Gopal A, Kumar D, Gopalkrishnan A, Pathak NN, Kurade NP, Tandan SK, Kumar D. Topical pluronic F-127 gel application enhances cutaneous wound healing in rats. *Acta Histochemica*. 2014;116(1):5-13.
- 46. Yuhua S, Ligen L, Jiake C, Tongzhu S. Effect of Poloxamer 188 on deepening of deep second-degree burn wounds in the early stage. *Burns*. 2012;38(1):95-101.
- Batrakova EV1, Kabanov AV. Pluronic block copolymers: evolution of drug delivery concept from inert nanocarriers to biological response modifiers. *Journal of Controlled Release*. 2008;10;130(2):98-106.
- 48. Dogan A, Demirci S, Caglayan AB, Kılıc E, Gunal MY, Uslu U, Cumbul A, Sahin F. Sodium pentaborate pentahydrate and pluronic containing hydrogel increases cutaneous healing *In Vitro* and *In Vivo*. *Biological Trace Element Research* . 2014;162:72-79.
- 49. Buke Ç. Current treatment of diabetic foot infections and the effect of Dermobor. *Cyprus Journal of Medical Sciences*. 2017; 2: 29-34.
- 50. Aysan E. Clinical Trials Website 2019 [cited 2019 October 10]. Available from: https://clinicaltrials.gov/ct2/show/NCT02241811?cond=Sodium+Pentaborate&rank=1
- Aysan E, Idiz UO, Elmas L, Saglam EK, Akgun Z, Yucel SB. Effects of boron-based gel on radiation-induced dermatitis in breast cancer: a double-blind, placebo-controlled trial. *Journal of Investigative Surgery*. 2017;30(3):187–192.
- 52. Cuadrado TM, WHO ATC Classification System; [cited 2018 02 July ]. Available from: https://ec.europa.eu/cefdigital/wiki/pages/viewpage.action?pageId=52609352.
- Tavelli B, I need your idea; [cited 2019 19 July]. Available from: https://tr.surveymonkey.com/r/LP8BGNT.
- 54. IQVIA Data On File, Retail and Hospital Annual Sales/RX Report. 2019.

55. Selami D, Aysegül D, Emre K, Zekai H, Atila T, Elif D, Fikrettin S. Boron and poloxamer (F68 and F127) containing hydrogel formulation for burn wound healing. *Biolog Trace Element Research*. 2015; 168:1-12.

