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Bölüm 1

DERMOKOZMETİK ÜRÜNLERDE BULUNAN DOĞAL KAYNAKLI HAMMADDELER

Elif ERDÖNMEZ[1]
Hafize YUCA[2]

GİRİŞ

Sağlıklı yaşam, bedenen ve ruhen sağlıklı, iyi, mutlu hissettiren bir yaşam şeklidir. Son zamanlarda sağlıklı yaşam ideali ile birlikte, doğal ve bitkisel ürünlere ilgi çok artmıştır. İnsanlar sağlıklı bir ömür için bitkisel ilaçlara ve doğal tedavi uygulamalarına öncelik vermektedir. Sentetik kimyasalların, boyaların ve sentetik bazlı ürünlerin çok fazla kullanımı, istenmeyen yan etkilerle seyreden çok sayıda hastalığa neden olmakta ve insan sağlığına zarar vermektedir. Üstelik bu kimyasalların kullanımı ekosistemin düzenini bozmakta ve çevre kirliliğine de yol açmaktadır. Bu nedenle bitkisel kozmetiklere ve kişisel bakımda bitkisel kozmetiklerin kullanımına ilgi giderek artmaktadır. Kozmetik alanında kullanılan aktif biyoaktif bileşenlere sahip fitofarmasötikler bitkisel kozmetikler preparatlarını temsil etmektedir. Farklı tıbbi bitkilerden elde edilen bu bitkisel kozmetiklerin iki önemli fonksiyonu vardır: Birincisi vücut ve vücut bölümlerinin bakımını kozmetik olarak düzeltmekte; ikincisi ise cilt veya saç için gerekli besinleri temin ederek biyolojik işlev göstermektedir. Büyük bir hızla büyüyen kişisel bakım endüstrisinde ilerleyen yıllarda bitkisel içerikli kozmetiklere daha fazla önem verilecektir. Bitkisel kozmetikler Amerikan Gıda ve İlaç Dairesi (FDA) mevzuatı kapsamında incelenmez. Güvenilirlikleri açısından kozmetiklerde de olduğu gibi her ülkenin var olan kurallarına göre değerlendirilir (1).

Dermokozmetik ürünlerde doğal kaynaklı maddelerin ve bitkisel ekstrelerin kullanımı, drog çeşitliliği giderek artmakta ve gelecek yıllarda da bu ürünlerin kullanımının daha popüler hale gelmesi beklenmektedir.

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Bölüm 2

DERMATOLOJİDE TIBBİ BİTKİLERİN ÖNEMİ

Benan KALAYCI[1]

GİRİŞ

Deri, insan vücudunun en büyük organı olarak kabul edilir ve organizmayı dış ortamdan izole etmek için koruyucu bariyer görevi görmektedir. Fiziksel, kimyasal, mikrobiyal ve immünolojik faktörler çeşitli dermatolojik bozukluklara yol açabilir (1).

Dermatolojide akne, alopesi, dermatit, bakteriyel, viral ve fungal cilt enfeksiyonları, cilt kanseri, psöriazis, vitiligo, yara ve yanıklar için bitkisel tedaviler kullanılmaktadır (2). Tıbbi bitkiler, içerdikleri etkili bileşiklerden dolayı çeşitli cilt hastalıklarının tedavisinde ve semptomlarının hafifletilmesinde faydalı olmaktadır.

DERMATOLOJİDE KULLANILAN TIBBİ BİTKİLER

Tedavi edici etkileri nedeniyle dermatolojide kullanımı olan *Rosmarinus officinalis* L., *Aloe vera* (L.) Burm. f., *Allium cepa* L., *Glycyrrhiza glabra* L., *Melaleuca alternifolia* (Maiden & Betche) Cheel, *Centella asiatica* (L.) Urban., *Nigella sativa* L., *Matricaria chamomilla* L., *Hypericum perforatum* L., *Avena sativa* L., *Triticum aestivum* L., *Echinacea purpurea* (L.) Moench, *Simmondsia chinensis* (Link) C.K. Schneider, ve *Hamamelis virginiana* L. bitkileri ve bu bitkilerin dermatolojik hastalıklardaki tedavi edici etkileriyle ilgili bilimsel çalışmalar aşağıda özetlenmiştir.

Rosmarinus officinalis L.

Rosmarinus officinalis L. (Lamiaceae), "biberiye" olarak bilinen ve Akdeniz'e özgü bir bitki olup, tüm dünyada yetiştirilmektedir. Bitkinin yaprakları kafeik asit türevleri (rosmarinik asit), diterpenler (karnosolik asit, izorosmanol, rosmadial), flavonoitler (diosmin, hesperidin), triterpenler (oleanolik asit, ursolik

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Bölüm 3

HELICHRYSUM PLICATUM SSP. *PLICATUM* BİTKİSİNİN FARMAKOLOJİK AÇIDAN DEĞERLENDİRİLMESİ

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GİRİŞ

Helichrysum Gaertner (Asteraceae) türleri, halk arasında yüzyıllardır enfeksiyon, yara, diyabet ve solunum rahatsızlıklarının tedavisinde geleneksel olarak kullanılmaktadır (1). Dünyanın birçok yerinde farklı bölgelerde *Helichrysum* türleri çeşitli kullanımlara sahiptir. Güney Afrika Kwazulu-Natal'da, *H. aureonitens* Sch.Bip. türünden elde edilen ekstrelerin halk arasında deri enfeksiyonlarında ve zona tedavisinde, *H. nudifolium* (L.) Less. türünün ise baş ağrısı ve yangılı hastalıkların tedavisinde kullanıldığı bilinmektedir (1,2). *H. arenarium* (L.) Monech türünün çiçekleri ise Avrupa' da tıbbi amaçla hazırlanan bitki karışımlarında görünümü iyileştirmek için eklenmekte ve uzun yıllardır kullanılmaktadır. Avrupa'da halk tarafından *H. arenarium* ve *H. italicum*'un kapitulumlarından hazırlanan çaylar, safra düzenleyici özelliklerinden dolayı kronik safra kesesi iltihabının tedavisine yardımcı (3)ayrıca *H. arenarium*; sarılık, gut, romatizma, sistit, artrit ve böbrek rahatsızlıklarında ve vücutta ödem varlığında idrar söktürücü olarak kullanılmaktadır (4,5). *H. odoratissimum* (L.) Sweet, Rwanda'da halk ilacı olarak egzama, menstüral ağrı ve kısırlık; Kenya'da yanık ve konjonktivit, Güney Afrika'da ise öksürük ve soğuk algınlığı, karın ağrısı ve mide rahatsızlıklarının tedavisinde kullanılmaktadır (6,7).*H. litoreum* türünün "Tabakazzu" olarak adlandırılan kurutulmuş çiçek durumları sigara şeklinde içilerek bronşiyal astımda, ezilmiş şeklinin dişe uygulanmasıyla da diş ağrılarının tedavisinde kullanılmaktadır(8).

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mide bulantısı görülürken karbosistein alanlarda %9,09 (6/66) oranda mide bulantısı görülmüştür. Koruyucu öksürük şurubu alanlarda uyuşukluk hali görülmezken karbosistein alanlarda %3,03 (2/66) oranda görülmüştür. Koruyucu öksürük şurubu alanlarda %1,33 (1/75) oranda kızarıklık görülürken, karbosistein alanlarda %1,52 (1/66) oranda kızarıklık görülmüştür (49).

SONUÇ

Ülkemizde doğal olarak yayılış gösteren, etnobotanik kullanımının yanı sıra Anadolu'da geleneksel halk ilacı olarak yüzyıllardır çeşitli hastalıkların tedavisinde kullanılan *H. plicatum* ssp. *plicatum* bitkisinin biyolojik aktivitelerinin belirlenmesi ve içerdiği maddelerin ortaya konulması oldukça önemlidir. Bu amaçla, özellikle *H. plicatum* ssp. *plicatum* bitkisi bazında farklı *Helycrysum* türlerinin biyolojik aktiviteleri, literatürde yer alan *in vitro*, *in vivo* ve klinik çalışmalar incelenerek derlendi. Bu bitkinin Ülkemizde halk arasında yaygın kullanımı bulunmakla birlikte bitkiyle ilgili araştırmaların oldukça az olduğu görüldü. Halk arasındaki tıbbi amaçlı kullanıma paralel birçok çalışma literatürde yer alsa da bitkinin biyolojik aktivitelerini ve etki mekanizmalarını tam olarak ortaya koyabilmek ve etkiden sorumlu maddeleri ortaya çıkarabilmek için daha fazla sayıda *in vitro*, *in vivo* ve klinik çalışmanın yapılması gerektiği sonucuna varıldı. Bu çalışmada, halk arasında sıklıkla kullanılan ve daha çok "ölmez çiçek" adı ile bilinen, ülkemize endemik *H. plicatum* ssp. *plicatum* bitkisinin, literatürde yer alan biyolojik aktiviteleri ve fitokimyasal içeriğiyle ilgili çalışmaları derlenmiştir. Araştırmacılara bu açıdan yön göstermeye yardımcı olabileceği düşünülmektedir.

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Bölüm 4

PRİMER DİSMENORE TEDAVİSİNDE KULLANILAN DESTEKLEYİCİ TIBBİ BİTKİLER VE MİKRO BESİNLER

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GİRİŞ

Menstrüasyon ile ortaya çıkan ağrılı kramplar olarak tanımlanan dismenore, yaş ve ırktan bağımsız en sık görülen jinekolojik sorundur. (1) Primer dismenore ile ilişkili en güçlü semptomlar, alt karın ağrısı ve lumbagodur. Bu ağrılara ek olarak baş ağrısı, baş dönmesi, yorgunluk, ishal, kramplar ve terleme gibi çok çeşitli fiziksel semptomlar gözlenmektedir. (2,3) Birçok kadın için güçten düşürücü bir durumdur ve kişinin yaşam kalitesi, iş verimliliği ve sağlık hizmeti kullanımı üzerinde önemli bir etkisi vardır. (4) Dismenore birincil ve ikincil olmak üzere iki tipe ayrılır. Primer dismenore, altta yatan bir patoloji olmaksızın menstrüasyon dönemindeki ağrıyı ifade ederken, sekonder dismenore altta yatan patolojiyle ilişkili ağrılı menstrüasyonu ifade eder. (5) Pelvik muayene, ultrason ve/veya tanısal laparoskopi olmadan primer ve sekonder dismenore tamamen ayırt edilemez ve bu iki tip benzer semptomatik tedavi yaklaşımlarını paylaşır. (6) Primer dismenorenin nedenleri hala belirsizdir, ancak en çok kabul edilen açıklamalardan biri, prostaglandinlerin (PG) sentezinin artmasıdır bu da ritmik olmayan uterus kasılmalarına ve kan akışının azalmasına neden olur. (7)

Primer dismenore tedavisinde farmakolojik, non-farmakolojik ve cerrahi olmak üzere üç yaklaşım tipi vardır. (8) Farmakolojik tedavilerin amacı, menstrüasyon dönemindeki ağrı ve menstrüasyon dönemi ile ilişkili sistemik etkilerden sorumlu PG'lerin ve lökotrienlerin (LT) üretimini azaltmaktır. Birinci basamak tedaviler, NSAİİ ve/veya OK kullanımı yoluyla PG'lerinve LT'lerin seviyelerinin azaltılmasını amaçlar. (9) En sık kullanılan farmakolojik ajanlar

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kisini araştıran daha fazla klinik çalışma olduğu göstermektedir. Bu durumda bize bitkilerin kullanılabilirliği için bize daha fazla kanıt sunmaktadır.

Mikro besinler vücudun fizyolojik işlevini gerçekleştirmek ve korumak için gereklidir. Eksikliği insan sağlığı üzerinde birden fazla mekanizmanın bozulmasına yol açar. Bu çalışmada araştırılan vitaminler (E, D, K, B1), mineraller (çinko, kalsiyum, magnezyum) ve omega-3 yağ asitlerinin primer dismenore üzerinde etkili olduğu görülmektedir. Bu mikro besinler anti-enflamatuar ve analjezik aktivetelerde rol alarak hastalarda rahatlama sağlamaktadır. En fazla klinik çalışma E ve D vitaminleri ile omega-3 yağ asidi için bulunmaktadır.

Bu çalışmada bahsi geçen tıbbi bitki ve mikro besinlerin primer dismenoreде potansiyel etkilerinin olduğu görülmektedir. Bu tıbbi bitki ve mikro besinlerin etkinliğini ve güvenliğini doğrulamak, etki mekanizmalarını açıklamak, etkin dozunu belirlemek ve yan etkilerini açıklamak için daha fazla çalışmaya ihtiyaç duyulmaktadır.

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Bölüm 5

BROMELAİN VE TERAPOTİK KULLANIMI

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GİRİŞ

Bromelain, *Bromeliaceae* familyasından olup, *Ananas comosus'un* elde edilen endopeptidazlarla ilişkili sülfidril proteolitik enzimdir. Bromelain bitkiden elde edildiği bölgeye göre meyve veya gövde bromelaini olarak isimlendirilir (1). Özellikle kök kısmının yüksek bromelain içermesinin yanı sıra düşük toksisite, yüksek verimlik ve kolaylıkla elde edilmesi nedeniyle enzimin ticari olarak geliştirilmesine ve bitkisel tıbbi bileşik olarak kullanılmasına yol açmıştır (2). Bromelain, membran filtrasyonu, rekombinant DNA teknolojisi ve mikro çoğaltma işlemleri gibi farklı yöntemlerle izolasyonu yapılarak büyük ölçekli üretilmektedir (3). Yapılan araştırmalarda anti-inflamatuar, antimikrobiyal, anti-tümöral, antitrombotik ve antikoagülan etkileri başta olmak üzere geniş bir farmakolojik etki profiline sahip olduğu ortaya çıkarılmıştır (4). Son yıllarda, transdermal su kaybını düzenlemesi, hücre yenilenmesini ve kolajen sentezini uyarması, sindirime yardımcı olması gibi spesifik özellikleriyle literatürdeki yerini almıştır. Günlük kullanım dozu 80-320 mg'dır. Günlük dozu 2000 mg/kg'ı geçmemelidir. Uygulamayı takiben bir saat içerisinde maksimum konsantrasyonuna ulaşır, ek olarak emilimi ve oral biyoyararlanımı da oldukça yüksektir (5). Biyoyararlanımındaki avantajları nedeni ile özellikle antibiyotiklerin absorpsiyonunu arttırma ile aşı ve anti-tümöral ajanların hazırlanmasında da kullanılmaktadır (6). Ayrıca, geniş pH aralığında aktivite göstermesi ve stabil kalması nedeniyle pepsin ve tripsin enzimlerinin eksikliğinde kullanımı mevcuttur (7). Ek olarak

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talarda bromelain uygulaması ise plasebo grubuna kıyasla hematom hacminde önemli bir azalma ile daha hızlı rezorpsiyon sağlamıştır. Buna göre kas-iskelet sisteminde spor yaralanmalarını da içeren künt travma vakalarında bromelain tedavisinin yaralanma bölgesinde ağrı, morarma, şişme ve kızarıklık üzerine iyileştirici etkili olduğu söylenebilir (46).

SONUÇ

Bromelain, çeşitli terapötik etkilere sahip güvenli bir gıda takviyesi olarak kullanılmaktadır. Oral kullanımı sonrasında yüksek biyoyararlanıma sahip olması ve düşük yan etki potansiyeli göstermesi nedeniyle metabolik hastalıklardan kanser tedavisine kadar geniş bir terapötik ağa sahiptir. Bu bağlamda bromelain kardiyovasküler hastalıklar, inflamatuar hastalıklar, spor yaralanmaları gibi çeşitli komplikasyonlarda etkili bulunmuştur. Preklinik ve klinik çalışmalar sonucunda anti-inflamatuar, antimikrobiyal, anti-tümöral ve immünmodülatör etkileri bulunmuştur. İncelenen çalışmalar ışığında etki mekanizması ve fonksiyonel özellikleri açısından bromelainin tıp ve sağlık alanında umut vaat ettiği düşünülmektedir. Yapılan araştırmalar bromelainin kardiyovasküler hastalıklardan kansere kadar çeşitli hastalıkların profilaktik ve terapötik tedavisinde etkili bir gıda takviyesi olarak kullanılabileceğini göstermektedir. Kapsamlı randomize kontrollü çalışmalar ile etkinliğinin ve güvenirliğinin doğrulanmasına ihtiyaç duyulmaktadır.

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Bölüm 6

EMODİN VE ANTİ-TÜMORAL ETKİSİ

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GİRİŞ

Günümüzde radikal bir tedavisi bulunamayan kanser, somatik hücrelerin anormal şekilde vücut içinde kontrolsüz çoğalması ve çok hızlı yayılım göstermesi ile karakterize olan, mortalite ve morbilitesi yüksek bir hastalıktır. Son yıllarda en yaygın görülen kanser türleri erkeklerde akciğer, prostat ve mide kanseri olarak kadınlarda ise meme, akciğer, Kolorektal ve serviks kanserleri olarak bilinmektedir (1). Kanser tedavisinde cerrahi yöntemler, radyoterapi ve kemoterapi gibi farklı tedavi stratejileri kullanılmaktadır. Ancak cerrahi yöntemler metastatik yayılmalara veya tekrarlayan lokal primer tümörlere neden olabildiğinden cerrahi müdahale öncesi ve sonrasında kemoterapötik ajanlar uygulanmaktadır (2). Bitki kaynaklarından elde edilen kemoterapötik ajanlar geçmişten günümüze kadar geleneksel tedavi yöntemleri arasındaki yerini korumaktadır (3).

Geleneksel Çin Tıbbı'ında kullanılan Emodin (1,3,8-trihidroksi-6-metil-antrakinon) *Rheum* bitki türlerinden elde edilen bir antrokinon türevidir (4-7). Emodin geniş etki profiline sahip olup anti-tümoral, anti-inflamatuar, antiviral, antibakteriyel, anti-alerjik, antidiyabetik, neroprotektif, hepatoprotektif ve immünosupresif etkiler göstermektedir (8, 9). Ayrıca ülser tedavisinde, kronik kabızlık vakalarında ve laksatif özelliği nedeniyle kilo almayı önleyici yöntemlerde kullanılmaktadır (10). Son yıllarda yapılan *in vivo* ve *in vitro* araştırmalar emodinin apoptotik hücre ölümünün indüksiyonu, proliferasyon ve hücre döngüsünün inhibisyonu gibi çeşitli etki mekanizmalarına sahip olduğunu göstermiştir

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Bölüm 7

MAJİSTRAL İLAÇLARA GÜNCEL BAKIŞ: LEKE TEDAVİSİNDE KULLANILAN REÇETELER

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GİRİŞ

Deri, vücudun fizyolojik durumunu etkileyebilecek mekanik, kimyasal ve mikrobiyal faktörlere karşı etkili fiziksel bariyer sağlayan bir vücut örtüsü olup, vücudu ultraviyole ışınlardan ve diğer çevresel etkenlere karşı savunmada önemli bir rol oynamakla birlikte pigmentasyonda görev alan melanin pigmentini içerir. Genetik olarak belirlenen ve çeşitli düzenleyici faktörler ile değişebilen melanin seviyesini yansıtan pigmentasyon; artması (hiperpigmentasyon) veya azalması (hipopigmentasyon) durumunda deride leke oluşumuna zemin hazırlamaktadır.

İlaç üretiminde sanayileşmeye rağmen, hastaya özgü ilaç hazırlama gerekliliklerini güncelliğini korumakta olup; hazır olarak üretilmeyen preparatların eczanelerde hazırlanması, az miktarda üretim, hastaya uygun tedavi, hasta uyuncunu arttırmak, tedavide kullanılacak olan ilacın piyasada müstahzarı olmadığı veya ithal ürün olduğu için pahalı olduğu durumlar gibi nedenlerden dolayı, eczanelerde majistral ilaç yapımı güncel olarak devam etmektedir.

Bu çalışma kapsamında 2021-2022 yılları arasında Adana ilinde bulunan merkez ilçelerdeki eczanelere gelen, dermatologlar tarafından leke tedavisi amacıyla reçete edilmiş majistral ilaçlar derlenmiştir. Güncel olarak leke tedavisinde sıklıkla kullanılan etken maddeler ve bu etken maddelerin etki mekanizmaları özetlenmiş olup, leke tedavisi için reçete edilen topikal formülasyonların içerikleri, hazırlanması ve kullanımları sunulmuştur.

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akne vulgaris tedavisinde kullanılmakta olup postenflamatuar hiperpigmentasyonu da etkili bir şekilde tedavi ettiği klinik çalışmalarda gösterilmektedir (19, 21). Adapalen, tretinoinden daha az tahrişe neden olduğu için tretinoini tolere edemeyen hastalarda kullanılabilmektedir (Reçete No: 18).

SONUÇ

İnsan derisi, fizyolojik ve çeşitli çevresel faktörlerin etkisiyle pigmentasyon bozukluğuna uğrayabilmektedir. Hastanın yaşam kalitesini arttırmak amacıyla pigmentasyon bozukluklarının tedavi edilmesi gerekmektedir. Hipopigmentasyon ve hiperpigmentasyon şeklinde görülen bu bozukluklar oral, topikal ve lazer tedavileri yöntemleri kullanılarak ortadan kaldırılabilmekte veya azaltılabilmektedir. Bu yöntemler arasında sıklıkla tercih edilen yöntem, topikal tedavi olup yarı katı dozaj formları kullanılmaktadır. Piyasada bulunan müstahzarların yanı sıra kişiye özgü tedavi, kombinasyon tedavisi ve hasta uyuncunu artırmak amacıyla majistral ilaçlar da tercih edilebilmektedir. Bilimsel çalışmalar ışığında, kanıta dayalı veriler kullanılarak hazırlanan majistral ilaçlar, ticari müstahzarlarla kıyaslandığında pek çok avantaj sağladığı görülmektedir. Hastanın durumuna ve ihtiyacına yönelik hekim tarafından reçete edilen bu formülasyonlar, hazırlama prosedürüne uygun şekilde eczanelerde eczacı tarafından hazırlanarak hastaya sunulmaktadır. Özellikle leke oluşumu gibi kompleks ve farklı mekanizmaların bulunduğu hastalıklarda kişiselleştirilmiş tedavinin kullanılması önemini korumaktadır.

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Bölüm 8

OKÜLER HASTALIKLARIN TEDAVİSİ İÇİN HİDROJEL BAZLI İLAÇ TAŞIYICI SİSTEMLER

Heybet Kerem POLAT[1]

GİRİŞ

Göz, vücudun en izole, eşsiz ve karmaşık yapıya sahip organlarından biridir ve anterior(ön) ve posterior (arka) olmak üzere iki kısımdan oluşur. Anterior segment; kornea, konjonktiva, aköz hümör, iris, siliyer cisim ve kristalin lensten oluşurken, posterior segment ise sklera, koroid ve retina pigment epiteli gibi kısımlardan oluşmaktadır (1). Oküler hastalıklar, bireylerin yaşam kalitesini doğrudan etkilemektedir. Son bir rapora göre, 2020'de dünya çapında 596 milyon insanın uzağı görme bozukluğuna sahip olduğu ve 43 milyon kişinin ise kör olduğu tahmin edilmektedir. Görmeyi önemli ölçüde etkileyen katarakt, kuru göz sendromu (DES), glokom, üveit, yaşa bağlı makula dejenerasyonu (AMD), diyabetik retinopati (DR) ve retinal ven tıkanıklıkları (RVO) gibi anterior ve posterior hastalıklar bulunmaktadır. Bu hastalıkların çoğu katarakt hariç (lens çıkarılıp sentetik lensler ile değiştirilmektedir) ilaçlar ile tedavi edilmektedir (2).

Genel olarak, ön segment hastalıklarının tedavisinde göz damlalarının topikal uygulanması tercih edillirken, arka segment hastalıklarından intravitreal enjeksiyonlar sıklıkla kullanılmaktadır. Oküler göz damlaları sıklıkla tercih edilmesine rağmen, oküler kavitenin küçük yapısı, nazolakrimal drenaj, prekorneal eliminasyon, konjonktival absorpsiyon ve zayıf retansiyon süresi, ilaçların oküler biyoyararlanımını ve terapötik etkinliklerini azaltmaktadır. Azalan biyoyararlanımı artırmak için günlük uygulama sıklığının artırılması gerekmektedir, bu durum da hasta uyuncunu azaltmaktadır (3). İntravitreal enjeksiyon ise anterior kısma ilaç uygulama açısından tekrarlayabilirlik sağlasa da bu enjeksiyonun sık uygulanması hastalar açısından rahatsız edicidir ve ciddi anlamda retina dekolmanı ve endoftalmi riski oluşturmaktadır (4). Bu nedenle, oküler hastalıkların tedavisi için uzun etkili formülasyon geliştirmek, hedeflenen anahtar stratejilerden biridir.

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SONUÇ

Son yıllarda, *in situ* hidrojel, kontakt lens ve hidrojel oluşturucu mikroiğneler dahil olmak üzere çok çeşitli hidrojeller anterior segment hastalıklarının tedavisi için geliştirilmiştir. Genel olarak, hidrojelin (i) prekorneal yüzey alanında kalma süresini uzatma, (ii) uygulama bölgesinde ilaç salımını kontrol etme veya sürdürme, (iii) birden fazla ilacın birlikte verilmesi potansiyelini kanıtladığı söylenebilir. Ayrıca, birçok hidrojel bazlı oftalmik formülasyon, özellikle *in situ* hidrojeller, piyasada veya klinik denemeler altındadır.

Çok ilerleme kaydedilmiş olmasına rağmen, araştırmaların çoğu küçük moleküllü ilaçların topikal verilmesine odaklanmıştır. Özellikle, düşük stabilitesi ve kısa yarı ömrü olan ialçların uygulanmasında bazı sınırlamalara sahiptir. Bununla birlikte, hidrojeller ağ yapısındaki hareketliliklerini sınırlayarak ilaçların stabilitesini iyileştirmek ve ilaçların kontrollü/sürekli salım yoluyla dozlama sıklığını azaltmak dahil olmak üzere, özellikle retinaya uygulanacak ilaçların önündeki mevcut sınırlamaların üstesinden gelmek için büyük bir potansiyel olabilir. Uzun etkili hidrojellerin klinik uygulanabilirliğini kolaylaştırmak, endüstriyel ölçek büyütme ve üretim yapma, depolama koşulları ve uzun vadeli göz içi güvenliği ile ilgili konuların bilim adamları tarafından ele alınması gerekmektedir.

Özetle, geleneksel oftalmik dozaj formlarının sahip olduğu sınırlamalarının üstesinden gelme kabiliyeti nedeniyle, hidrojel bazlı oftalmik ilaç taşıyıcı sistemlere ilgi artmakta, artan sayıda ticarileştirilmiş hidrojel bazlı oftalmik ürün klinik deneylerden geçmektedir. Özellikle, retina hastalıklarının tedavisi için etkin maddeleri gözün arkasına iletmek ve klinik uygulamalarını teşvik etmek için hidrojeller üzerinde çalışmalar devam etmelidir.

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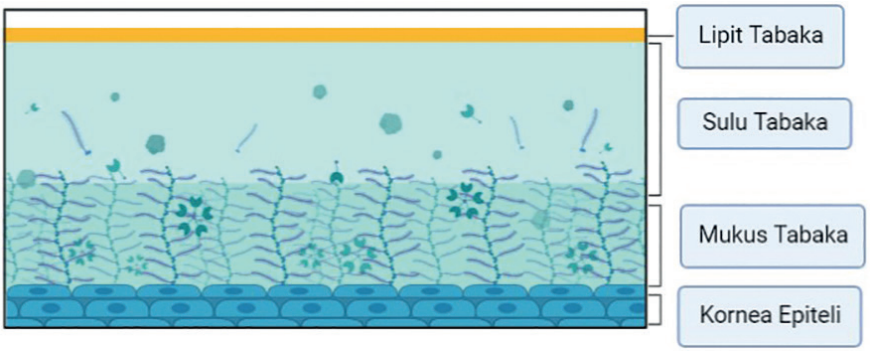
Bölüm 9

KURU GÖZ TEDAVİSİ İÇİN İLAÇ TAŞIYICI SİSTEMLER

Heybet Kerem POLAT[1]
Nihat KURT[2]

GİRİŞ

Gözyaşı sıvısı lipit, sulu ve müsin tabaka olmak üzere üç kısımdan oluşmaktadır (Şekil 1). 0.1 µm kalınlığa sahip olan lipit tabakası, gözyaşı sıvısının buharlaşmasını engellemektedir. 7-8 µm kalınlığa sahip orta sulu tabaka, gözyaşı filminin büyük kısmını oluşturmaktadır. İç müsin tabakası ise 0.2 µm kalınlığındadır. Kuru göz sendromu (KGS), aşırı gözyaşı buharlaşması veya gözyaşı eksikliğini içerebilen çeşitli genetik ve/veya çevresel faktörler oluşabilmektedir. KGS, keratokonjonktivit, hipofonksiyonel gözyaşı sendromu, oküler yüzey hastalığı, skarlaşma sendromu ve skarlı keratit olarak da bilinmektedir (1).



Şekil 1. Oküler yüzeyin şematik diyagramı.

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kullanan bir oftalmik süspansiyondur. Klinik çalışmalarda, KPI-121'in plaeboya kıyasla KGS belirtilerini önemli ölçüde azalttığı gösterilmiştir. KPI-121 %0,25, 2020 yılında FDA tarafından onaylanmıştır (80).

SONUÇ

KGS'yi tedavi ederken fizyolojik işlev üzerinde asgari düzeyde etkiye sahip etkili yöntemlerin geliştirilmesine ivedilikle ihtiyaç vardır. Yeni ilaçların ve kolloidal taşıyıcı sistemlerin ortaya çıkmasıyla KGS için daha etkili tedaviler sağlanacaktır. Nanoteknoloji, kozmetik, rejeneratif tıp, teşhis, İTS ve yeni ilaçlar için çok yönlü bir araçtır. Anterior göz hastalıklarının tedavisi için mevcut oftalmik formülasyonlardaki sınırlamaların üstesinden gelebilmek için nanoteknoloji bazlı yaklaşımların tasarımındaki son gelişmeler kayda değerdir. Bazı nanoterapötiklere FDA onayı verilmiştir ve çok daha fazlası klinik çalışmalarda veya geliştirilme safhasındadır. Oftalmik ilaçlar için nanoformülasyonların kullanımı ümit vericidir ancak ölçek büyütme, biyouyumluluk, formülasyon stabilitesi, ilaç salımı ve farmakokinetik ile ilgili hususları araştırmak için ek çalışmalara ihtiyaç vardır.

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Bölüm 10

CİLT HASTALIKLARINDA KULLANILAN JEL TİPİ DOZAJ ŞEKİLLERİNE GÜNCEL BİR BAKIŞ

Şeyma ASAN[1]
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GİRİŞ

İnsanların sağlık sorunlarının çeşitlenerek artmasında dünya nüfusundaki artış, toplumlardaki refah seviyelerinin yükselmesi, demografik özelliklerle ihtiyaç ve taleplerin değişmesi etkin rol almaktadır. İlaçlar geçmişte olduğu gibi günümüzde de sağlığın korunması veya sağlıklı halin devam ettirilmesi açısından her zaman önemini korumaktadır. İlaçlarla ilgili araştırma ve geliştirme çalışmaları hız kesmeden devam etmekte ve farmasötik teknolojinin ilerlemesiyle de hem uygulama yollarında hem de dozaj şekillerinde konvansiyonelden yeni nesile geçiş görülmektedir. Günümüzde çevresel faktörler (güneş, hava kirliliği, radyasyon vb.) ve beslenme şekillerindeki/kaynaklarındaki bozukluklar gibi nedenlerden dolayı cilt hastalıklarında ciddi bir artış görülmektedir. Bu artışla beraber tedavide/tedavi araçlarında verimliliğin ve etkinliğin artırılması için yeni yollar aramaya gidilmesi kaçınılmazdır. Cilt hastalıklarında topikal uygulama her zaman ilk tercih edilen yollardan biri olmuştur. Ancak gün geçtikçe tedavide etkinliğin artırılması amacıyla sürekli yeni nesil yarı katı dozaj şekilleri denenmekte ve ilaç piyasasında yer alması sağlanmaktadır. Kremler, merhemler, losyonlar ve jeller gibi yarı katı dozaj şekilleri sıklıkla topikal tedavide tercih edilmekle birlikte ilaç endüstrisinde üretimde ve ilaç pazarında da satışta büyük bir paya sahiptir. Bu bölümde jellerle ilgili güncel bilgiler bulunmaktadır.

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Bölüm 11

KANSER TEDAVİSİNDE ENJEKTE EDİLEBİLİR HİDROJEL İLAÇ TAŞIYICI SİSTEMLER

Dilara ÖRGÜL[1]

GİRİŞ

Günümüzde kanser, kalp hastalığını geride bırakarak dünya çapında önde gelen ölüm nedeni haline gelmiştir. Dünya kanser raporuna göre 2008 yılında yaklaşık 7,6 milyon kişi kanserden hayatını kaybederken 2020 yılında bu sayı %50 artmış ve yaklaşık 19,3 milyon yeni kanser vakası, 10 milyon kanser ölümü meydana gelmiştir (1). Kanser, genellikle kanser öncesi bir lezyondan habis bir tümöre ilerleyen çok aşamalı bir süreçte normal hücrelerin tümör hücrelerine dönüşmesinden kaynaklanır. Bu değişiklikler, bir kişinin genetik faktörleri ile dış etkenlerden kaynaklanmaktadır. Olağan sınırlarının ötesinde büyüyen ve daha sonra vücudun bitişik kısımlarını istila ederek diğer organlara yayılabilen anormal hücrelerin hızlı bir şekilde çoğalması süreci ise metastaz olarak adlandırılır. Yaygın metastazlar, kanserden ölümlerin birincil nedenini oluşturmaktadır. Her kanser tipi kendine özgü bir tedavi rejimine sahip olup mevcut klinik kanser tedavileri genellikle cerrahi, radyoterapi ve/veya sistemik tedaviyi (kemoterapi, hormonal tedaviler, hedefe yönelik biyolojik tedaviler) içermektedir (2). Ancak ne yazık ki, geleneksel kanser tedavi yaklaşımlarının çoğu normal hücrelere de zarar vererek ölümüne yol açmakta, bağışıklık sistemini yok etmekte ve ikinci bir kanser tanısının riskini artırmaktadır (3). Bu nedenle kaliteli, etkili ve güvenilir bir kanser tedavisinin uygulanması, erken teşhisle birlikte birçok kanser türünde hayatta kalma oranını artıran en önemli etkenlerden biri haline gelmiştir.

Hedefli ve kontrollü ilaç salım teknolojileri, belirli bir miktarda ilacın/ilaçların belirli bir zaman ve yerde salınmasına imkan sağlamaktadır. Kanser tedavisinde yeni ve kişiselleştirilmiş tedaviler sunmak için oldukça önemli olan bu teknolojiler sağladığı faydalar nedeniyle mevcut bilimsel tıbbi araştırmaların

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karşılaşılan bu sorunların üstesinden gelinmesi amacıyla enjekte edilebilir hidrojel formülasyonlarına olan ilgi artmıştır. Enjekte edilebilir hidrojeller iyi bir biyouyumluluğa, biyoparçalanabilirliğe, enjekte edilebilirliğe ve uyaranlara tepki verebilme özellikleri neticesinde ideal bir taşıyıcı sistem haline gelmişlerdir. Enjekte edilebilir hidrojellerin farklı uygulamaları arasında, kanser tedavisi ise en çok araştırılanlar alanlardan biridir. Sistemik uygulamalarla karşılaştırıldığında enjekte edilebilir hidrojeller, kanser tedavisinde; sağlıklı dokularda azaltılmış toksisite göstermesi, direk tümör bölgesine hedeflendirme ve bu bölgede uzatılmış salım imkanı sunması, daha etkili bir hücre apoptozunun yanı sıra artmış bir tümör büyüme inhibisyonunun da sağlanması gibi pek çok avantaj sunmaktadır. Bununla birlikte çeşitli kanser türleri ile gerçekleştirilen pek çok *in vivo* hayvan modeli çalışmasında, enjekte edilebilir hidrojellerle artmış bir antikanser etkinlik ve azaltılmış bir toksisitenin elde edilmesi oldukça umut verici sonuçlardır. Ancak ektopik tümör modelleri ile genellikle solid tümörler üzerinde gerçekleştirilen bu çalışmalarda tümöre özgü olan interstisyum tam olarak yansıtılamamaktadır. Bu nedenle antikanser etkinliğin daha doğru bir şekilde değerlendirilmesini sağlayacak hayvan modelleri üzerinde daha fazla çalışmanın gerçekleştirilmesi gerekmektedir. Bu yöndeki gelişmeler ve devam eden farmasötik teknoloji ve biyoteknoloji alanındaki ilerlemeler neticesinde enjekte edilebilir hidrojellerin, kanser tedavisinde klinik uygulamalara dahil edilme ihtimali artmaktadır.

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Bölüm 12

COVID-19 İLE İLİŞKİLİ DIABETES MELLITUS

Mehtap TUĞRAK SAKARYA[1]

GİRİŞ

SARS-CoV-2 virüsünün neden olduğu şiddetli akut solunum sendromuna neden olan Koronavirüs hastalığı (COVID-19), Mart 2020'de Dünya Sağlık Örgütü (WHO) tarafından küresel bir pandemi olarak ilan edildi. Bugüne kadar çok sayıda doğrulanmış vaka ve ölümle dünya çapında yayılmaya devam etmektedir (1).

Bu ölümcül virüsün yayılma hızı, dünya nüfusunun önemli bir bölümünün bundan etkileneceği konusunda hiçbir şüpheye yer bırakmayacak düzeydedir. Bu sebeple, COVID-19'un diğer yaygın olarak ortaya çıkabilecek olan tıbbi durumlarla nasıl bir etkileşiminin olduğunu tahmin etmek, bu konuda çözüm yolları bulmak ve bu tıbbi durumların yönetimi için bir protokole karar vermek büyük bir endişe konusu haline gelmiştir. Mevcut hastalardaki laboratuvar raporları değerlendirildiğinde, hemen hemen tüm raporlar yaygın bir bulgu olarak ciddi hipergliseminin varlığını göstermekte ve bu bulgu genellikle hastalık şiddetinin bir belirteci olarak kabul edilmektedir (2). Bu konu ile ilgili yapılan literatür araştırmaları COVID-19'un diyabeti olduğu bilinen ve hiç diyabet geçmişi olmayan kişilerde hiperglisemi ile ilişkili olduğunu göstermektedir (3,4). Bu nedenle, yapılan bu çalışmalar SARS-CoV-2 enfeksiyonunun COVID-19 hastalarında diyabetojenik bir duruma neden olduğu gerçeğini destekleyici niteliktedir (5,6). Bu çalışma ile COVID-19 hastalarında yeni başlayan diabetes mellitusun COVID-19 ile nasıl bir ilişkisi olduğu anlaşılmaya çalışılmıştır.

COVID-19'da SARS-CoV-2 Enfeksiyonunun Diyabetojenik Etkisi

COVID-19 hastalarında SARS-CoV-2 enfeksiyonunun diyabetojenik bir duruma yol açtığı artık iyi bilinen bir gerçektir. SARS-CoV-2 enfeksiyonu olan birçok hastaya COVID-19 sonrasında diyabet teşhisi konulduğunu bildiren çok sayıda

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Bölüm 13

ALKİL SÜBSTİTÜSYONUNUN FARMASÖTİK KİMYA AÇISINDAN ÖNEMİ

Mehmet KOCA[1]

GİRİŞ

Sübstitüent 'bir organik bileşikte, herhangi bir konumda bulunan hidrojen atomunun yerini alan atom veya atom grubu' şeklinde tanımlanmaktadır (1). Sübstitüentler dahil oldukları ana yapının bazı fiziksel (hacimsel, konformasyonel, vb) ve kimyasal (elektriksel, asitlik-bazlık, vb) özelliklerini değiştirerek ana yapının biyolojik aktivitesini etkilerler. Bir molekülün çözünürlüğü, lipofilisitesi, hedef yöreye ulaşabilmesi ve ilgili reseptörle etkileşimi o molekülün fizikokimyasal özellikleri ile ilişkilidir (2). Bir ana iskelete ait biyolojik aktivite tarama çalışmaları yapılırken en sık kullanılan sübstitüenler şunlardır: Alkil grupları (metil, dimetil, isopropil ve tert-bütil), π bağı içeren doyurulmamış gruplar (vinil, allil ve asetilenil), aromatik yapılar (fenil, tiyenil, furil, pirolo), halojenler (F, Cl, Br, I), karboksilik asitler, hidroksil, tiyol, amin ve nitro grupları (3).

Aşağıda gelecek olan alt konu başlıklarında ilk önce, bir ilacın biyolojik aktivitesinde lipofilisitenin, sterik yapının ve moleküldeki elektron dağılımının öneminden bahsedilecektir. Daha sonra ilaç araştırma-geliştirme çalışmalarında sıkça uygulanan alkil sübstitüsyonunun ana molekül üzerindeki sterik, elektronik, lipofilik etkileri ele alınarak alkil sübstitüsyonunun ana molekülün biyolojik aktivitesinde (farmakolojik aktivitesinde, toksisitesinde ve metabolizasyonunda) meydana getirdiği değişiklikler üzerinde durulacaktır.

ÜÇ TEMEL FİZİKOKİMYASAL ÖZELLİK

Lipofilisite

Lipofilisite, bir maddenin ortamdaki polar faza rağmen apolar bir faz içerisindeki dağılım davranışını ifade eder. Partisyon katsayısı lipofilisitenin önemli bir parametresidir (4). Nötral bir molekülün partisyon katsayısı genellikle Log P ile

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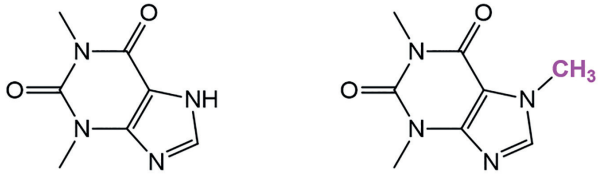

Şekil 23. Teofilin ve kafeinin kimyasal yapıları

SONUÇ

Alkil sübstitüsyonu ana molekülün sterik, elektronik, lipofilik özelliklerini etkileyerek ana molekülün kiralitesi, çözünürlüğü, iyonizasyonu ve pH'sı gibi birçoğu birbiriyle ilşkili olan fizikokimyasal özelliklerini değiştirir. Bu moleküler modifikasyonlar farmakolojik aktivite, toksisite ve metabolizasyon açısından molekülü tedavide daha avantajlı veya dezavantajlı bir hale getirebilir. Bu çalışma, küçük bir sübstitüent olan metil grubunun ilaç ar-ge ve molekül tasarım çalışmalarındaki önemini göstermektedir

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Bölüm 14

GASTROİNTESTİNAL DİSBİYOSİS VE HASTALIKLARLA ETİYOLOJİK İLİŞKİSİ

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GİRİŞ

Mikrobiyota vücudumuzdaki kommensal, patojenik ve simbiyotik mikroorganizmalardan oluşan kompleks bir komünitedir. Bu komünitenin içinde bakteri, arkea, virüs ve çeşitli ökaryotlar vardır . İnsan vücudunda bulunan insan hücrelerinin yaklaşık 9 katı kadar makroskobik konağa yerleşmiş mikrobiyal hücreler vardır ve bunların toplamı süperorganizma olan insanı oluşturur. Mikrobiyotayı oluşturan genlere "mikrobiyom" adı verilir (1). İnsan genomunda 35,000 gen varken, bakteriyel genom vücudumuzda 2 milyonu aşmaktadır (2). Mikrobiyota vücudumuzun farklı bölgelerinde bulunur ve fizyolojik ve metabolik işlevlerimizi yerine getirebilmemiz için elzemdir (3). Mikrobiyata vücutta oro-nazo-faringeal alan, göz, vajen, cilt, gastrointestinal sistem, amniyon sıvısı, üst solunum yolları ve akciğerler gibi farklı bölgelerde bulunur. Bu sistemlerden de en çok gastrointestinal sistemde ve onun en önemli bileşeni olan kolonda yoğun olarak bulunur (4, 5). Bağırsak mikrobiyotasının içeriği ve dağılımı kişiden kişiye değişir. Her insanın parmak izinin farklılığıgibi mikrobiyotası da farklıdır (6). Sağlıklı bireylerde bağırsak florasının yaklaşık olarak %90'ını gram pozitif bakterilerden *Firmicutes* ve *Actinobacteria* ve gram negatif *Bacteroidetes, Proteobacteria* bakterilerinden oluşturur (7). Floradaki bakteriler dinamik olup zararlı ve faydalı bakteri sayıları sürekli değişir. Faydalı bakteriler bir çok biyolojik ve kimyasal süreçte rol alırlarlar. Bağırsak mikrobiyotası, bağışıklık sisteminin desteklenmesi, gıdaların sindirimi, bazı vitaminlerin üretimi, metabolik reaksiyonlar, beyin faaliyetleri, bağırsak gelişimi, ideal vücut ağırlığının korunması gibi pek çok faaliyette rol oynar (8). Bağırsak mikrobiyotası beyinle doğrudan

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genotoksik etki ve metabolik etki gibi mekanizmaların yer aldığı kanıtlanmıştır. Bağırsak disbiyozisi, fibromiyalji gibi kronik ağrı sendromlarına da neden olabilmektedir. Son olarak, bağırsak mikrobiyotasının fonksiyonel aktivitesi ve bileşiminin değişmesi inflamatuvar bağırsak hastalıklarını tetiklemektedir. Bu nedenle, bağırsak mikrobiyotasının sağlıklı bir şekilde korunması ve dengelenmesi, vücudun genel sağlığı için önemlidir.

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Bölüm 15

BAKTERİYOFAJ TERAPİSİNİN ENFEKSİYONLARIN TEDAVİSİNDE DÜNÜ BUGÜNÜ YARINI

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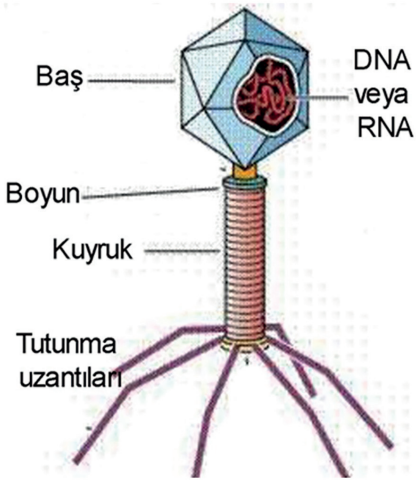
GİRİŞ

Bakteriyofaj

Bakteriyofajlar (faj) bakterilerin lizisine neden olan viruslerin genel adıdır. Şekil 1'de de görüldüğü gibi bakteriyofajların genel yapısı, DNA veya RNA'dan oluşan genetik materyal, onu çevreleyen protein kılıf ve tutunmayı sağlayan kuyruklardan oluşur (1). Bakteriyofajlar sulak alanlar, gübreli topraklar, sindirim sistemi, lağım suları gibi konakçısının bulunduğu her yerde bulunurlar (2).



Şekil 1. Faj morfolojisi (3)

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Faj terapisi kanser hastaları arasında yaygın olarak görülen *E. coli, P. aeruginosa, Klebsiella pneumoniae, Klebsiella oxytoca ve S. aureus* enfeksiyonlarına karşı antibakteriyel tedaviye yanıt alınamayan 20 hastaya uygulanmıştır. Araştırmacılar ağızdan günde üç doz faj alan hastaların hepsinin, tedaviyi takip eden ortalama 2 ila 9 haftalar arasında tamamen iyileştiğini belirtmişlerdir (109).

Fish ve arkadaşları tarafından gerçekleştirilen bir vaka serisi çalışmasında, tedavisi zor S. aureus enfeksiyonlu dokuz diyabetik ayak ülseri hastası, ticari olarak edinilebilecek bir Gürci stafilokok faj preparasyonu kullanılarak başarılı bir şekilde tedavi edilmiştir (110).

SONUÇ VE ÖNERİLER

Faj terapisi, çoklu ilaç dirençli bakterilerin neden olduğu toplum ve hastane kaynaklı infeksiyonlarla mücadelede eski fakat yeni bir alternatif tedavi yöntemi olarak daha da popüler hale gelmektedir. Faj terapisinin gerçek potansiyelinin ortaya konulabilmesi için doğru litik fajların seçilmesi, seçilen litik fajların iyi tanımlanması ve bu litik fajların biyolojilerinin iyi anlaşılmasına ihtiyaç vardır. Faj terapisiyle ilgili *in vitro* laboratuvar *in vivo* klinik çalışmalar arttırılarak terapinin gerçekten etkili olup olmadığı kanıtlanmalı ve şayet varsa terapinin yan etkileri araştırılmalıdır. Ayrıca, modern teknolojiler kullanılarak elde edilen verilerle toplum ve hastane kaynaklı infeksiyonlara neden olan çoklu ilaç dirençli bakterilere karşı bakteriyofaj ve antibakteriyel birlikteliğinin enfeksiyon tedavisindeki etkinliği ortaya konulmaya çalışılmalıdır. Halk sağlığı alanında bu konuyla ilgili araştırma projelerinin daha çok desteklenmesi önerilmektedir.

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