BÖLÜM 8

Uyaranlara Duyarlı Nanotaşıyıcılar

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Giriş

İlaç etkinliğinin genellikle spesifik olmayan hücre ve doku biyodağılımı ile değişmesi ve bazı ilaçların hızla metabolize olması veya vücuttan atılması nedeniyle hastalıklı bölgeleri verimli bir şekilde hedefleyen nanotaşıyıcı sistemlere olan ihtiyaç ortaya çıkmıştır. Malzeme bilimi ve eczacılık alanındaki ilerlemeler sayesinde, farklı boyutlara, mimarilere ve yüzey özelliklerine sahip çok çeşitli nanotaşıyıcı sistem tasarlanmıştır (1, 2). Bu taşıyıcıların küçük boyutları sistemik (örn., intravenöz) veya lokal (örn., mukozal) uygulamayı ve intraselüler difüzyonlarını kolaylaştırmayı mümkün hale getirmektedir. Ayrıca, mevcut yüzey işlevselleştirme yöntemleri kısmen de olsa nanotaşıyıcıların farmakokinetiğinin ve biyolojik dağılımının kontrol edilebilmesini sağlayabilir (3). Günümüzde onaylanmış ve pazarlanan nanotaşıyıcıların çoğu pasif hedeflendirme prensibi esas alınarak geliştirilmiştir (4). Pasif hedeflendirilmiş nanotaşıyıcılarda biyolojik yarı ömür uzamıştır, ancak bu sistemlerden erken ilaç salımı önemli bir dezavantajdır (3, 5).

Aktif hedeflendirme mükemmel bölgesel, zamansal ve dozaj kontrolü ile özel salım profillerini sağlayan isteğe bağlı süreçleri ("açma/kapama" olarak da adlandırılan) olanaklı kılmaktadır. Böylelikle, mikro çevrelerini tanıyan ve canlı organizmaların yanıt verebilirliğini taklit ederek dinamik tepkisellik göstererek uyaranlara yanıt veren sistemlerin tasarımı yoluyla programlanmış ilaç salımı mümkün hale gelmektedir (1, 5). Örneğin, hipertermi yoluyla ilaçların lokal salımı için sıcaklık-duyarlı lipozomların kullanılmasıyla

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Sonuç

Bu bölümde, endojen (pH, redoks, enzim), eksojen (sıcaklık, manyetik alan, ultrason, ışık, elektrik alan) ve çoklu uyaranlara duyarlı nano ilaç taşıyıcılar örneklerle ele alınarak incelenmiştir. İlaç taşıyıcı sistemlerin hedeflendirilmesinde uygulanan dozun çok az bir kısmı tümör bölgesine veya enfekte/enflamatuvarlı dokulara ulaşabilmektedir. Bu soruna çözüm bulabilmek amacıyla, aktif hedeflendirmeye odaklı malzeme geliştirilmesi çalışmaları ile birlikte, organizmadaki fizikokimyasal temelli değişikliklere yüksek hassasiyette yanıt verebilen, doğru yerde ve zamanda ilaç salımını mümkün hale getirecek farklı yapılardaki uyaranlara duyarlı nanotaşıyıcıların geliştirilmesi olanaklı hale gelmiştir. Ancak, başarılı *in vitro* çalışmaların sonuçlarına rağmen bu sistemlerden yalnızca birkaçı klinik çalışma safhasına geçebilmiştir. Ayrıca, tasarımlarındaki karmaşıklık ve ölçeklendirilmelerindeki güçlükler, bileşimlerine, fizikokimyasal özelliklerine ve uygulama yoluna bağlı toksisiteleri, çoğunun biyobozunabilir olmamaları veya yetersiz biyouyumlulukları bu sistemlerin uygulamalarını kısıtlamaktadır. Bu nedenle, söz konusu sorunların çözüme kavuşturulmasıyla uyaranlara duyarlı nanotaşıyıcılar klinik kullanımda yerlerini alabilecektir.

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