

# *İlaç taşıyıcı sistemler ve herbal drug*

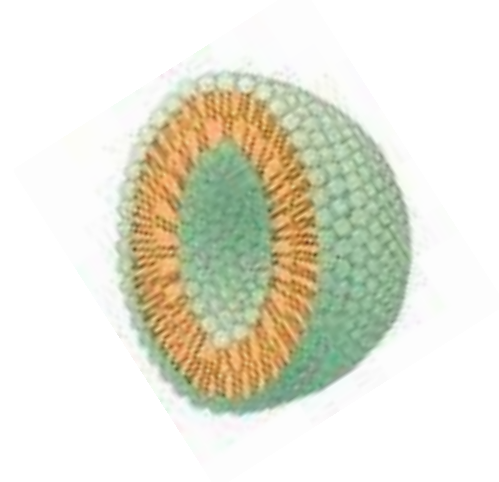
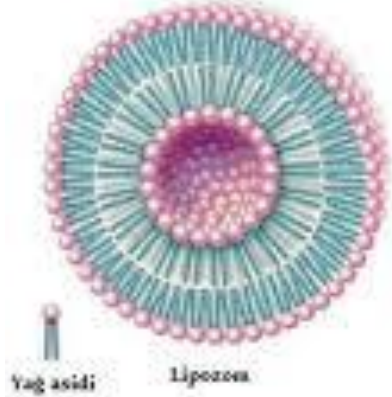


**14. Hafta**

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# İlaç taşıyıcı sistemler ve herbal drug

- Lipozomlar
- Aralarında sulu faz bulunan bir veya daha çok sayıda biyolojik membrana benzer yapıda çift lipid tabakalarının oluşturulduğu mikroskobik boyutlardaki küresel yarı katı cisimcikler/veziküllerdir.



# Lipozom

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- Çözünürlük artırarak biyoyararlanımı artırdığı için tercih edilir.
- *Slybum marianum: Slybin flavonoid*
- *Bukkal lipozomal veriliş ile biyoyararlanım artmış.*

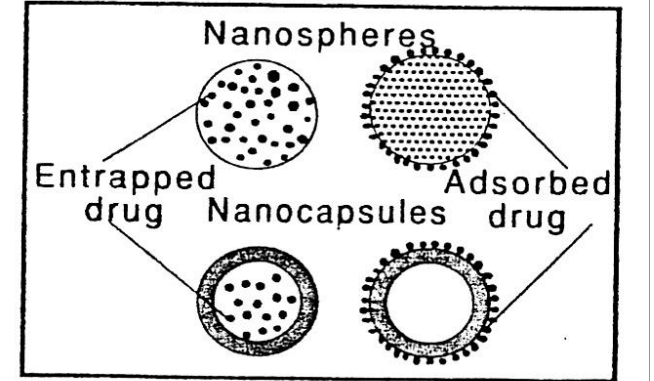
**Table 1**

Liposomal herbal formulation.

| Formulations                     | Active ingredients                  | Applications of liposome formulations   | Biological activity             | Method of preparation                                 | % Entrapment efficiency | Route of administration | Reference |
|----------------------------------|-------------------------------------|---|---------------------------------|---|-------------------------|-------------------------|-----------|
| Quercetin liposomes              | Quercetin                           | Reduced dose, enhance penetration in blood brain barrier                              | Antioxidant<br>Anticancer       | Reverse evaporation technique                         | 60%                     | Intranasal              | [18]      |
| Liposomes encapsulated silymarin | Silymarin                           | Improve bioavailability   | Hepatoprotective                | Reverse evaporation technique                         | 69.22 ± 0.6%            | Buccal                  | [16]      |
| Liposoma artemisia arborescens   | Artemisia arborescens essential oil | Targeting of essential oils to cells, enhance penetration into, cytoplasmatic barrier | Antiviral                       | Film method and sonication                            | 60–74%                  | In vitro                | [19]      |
| Ampelopsin liposome              | Ampelopsin                          | Increase efficiency   | Anticancer                      | Film-ultrasound method                                | 62.30%                  | In vitro                | [20]      |
| Paclitaxel liposome              | Paclitaxel                          | High entrapment efficiency and PH sensitive   | Anticancer                      | Thin film hydration method                            | 94%                     | In vitro                | [21]      |
| Curcumin liposome                | Curcumin                            | Long-circulating with high entrapment efficiency                                      | Anticancer                      | Ethanol injection method                              | 88.27 ± 2.16%           | In vitro                | [22]      |
| Garlicin liposome                | Garlicin                            | Increase efficiency   | Lungs                           | Reverse-phase evaporation method                      | 90.77 %                 | –                       | [23]      |
| Flavonoids liposomes             | Quercetin and rutin                 | Binding of flavonoids with Hb is enhanced   | Hemoglobin                      | Solvent evaporation                                   | –                       | In vitro                | [24]      |
| Usnea acid liposome with β-CD    | Usnea acid                          | Increase solubility and localization with prolonged-release profile                   | Antimycobacterial               | Hydration of a thin lipid film method with sonication | 99.5%                   | In vitro                | [25]      |
| Wogonin liposome                 | Wogonin                             | Sustained release effect  | Anticancer                      | Film dispersion method                                | 81.20 ± 4.20%           | In vivo                 | [26]      |
| Colchicine Liposome              | Colchicine                          | Enhance skin accumulation, prolong drug release and improve site specificity          | Antigout                        | Rotary evaporation sonication method                  | 66.3 ± 2.2%             | Topical                 | [27]      |
| Catechins liposomes              | Catechins                           | Increased permeation through skin   | Antioxidant and chemopreventive | Rotary evaporation sonication method                  | 93.0 ± 0.1              | Transdermal             | [28]      |
| Breviscapine liposomes           | Breviscapin                         | Sustained delivery of breviscapine  | Cardiovascular diseases         | Double emulsification process                         | 87.9 ± 3.1%             | Intramuscular           | [29]      |

# Nanopartiküller

- Nanopartiküller büyüklükleri 10-1000nm arasında değişen çözünmüş hapsedilmiş veya adsorbe olan etkin maddeyi kontrollu olarak salan katı kolloidal partiküllerdir.
- Yine partikül boyutunun küçülmesi sonucu çözünürlük artışına bağlı biyoyararlanım artışı



**Table 2**

Nano structured herbal formulations.

| Formulations                               | Active ingredients           | Applications of nanostructured formulations   | Biological activity  | Method of preparation                                  | % Entrapment efficiency       | Route of administration | Reference |
|--|------------------------------|---|--|--|-------------------------------|-------------------------|-----------|
| Triptolide nanoparticle                    | Triptolide                   | Enhance the penetration of drugs through the stratum corneum by increased hydration | Anti-inflammatory  | Emulsification-ultrasound                              | -                             | Topical (skin)          | [30]      |
| Nanoparticles of <i>Cuscuta chinensis</i>  | Flavonoids and lignans       | Improve water solubility,   | Hepatoprotective and antioxidant effects                           | Nanosuspension method                                  | 90%                           | Oral                    | [37]      |
| Triptolide-loaded solid lipid nanoparticle | Triptolide                   | Decreasing the toxicity   | Anti-inflammatory  | Emulsification-ultrasound                              | -                             | Oral                    | [38]      |
| Artemisinin nanocapsules                   | Artemisinin                  | Sustained drug release  | Anticancer   | Self-assembly procedure                                | 90-93%                        | In vitro                | [39]      |
| Radix salvia miltiorrhiza nanoparticles    | R. salvia miltiorrhiza       | Improve the bioavailability   | Coronary heart diseases, angina pectoris and myocardial infarction | Spray-drying technique                                 | Upto 96.68%                   | In vitro                | [40]      |
| Taxel-loaded nanoparticles                 | Taxel                        | Enhance the bioavailability and sustained drug release                              | Anticancer   | Emulsion solvent evaporation method                    | 99.44%                        | -                       | [41]      |
| Berberine-loaded nanoparticles             | Berberine                    | Sustained drug release  | Anticancer   | Ionic gelation method                                  | 65.40 ± 0.70%                 | In vitro                | [42]      |
| Silibini-loaded nanoparticles              | Silibini                     | High entrapment efficiency and stability  | Hepatoprotective   | High pressure homogenization                           | 95.64%                        | -                       | [43]      |
| Tetrandrine-loaded nanoparticles           | Tetrandrine                  | Sustained drug release  | Lung   | Self-emulsification and solvent evaporating            | 84%                           | In vitro                | [44]      |
| Glycyrrhizic acid-loaded nanoparticles     | Glycyrrhizic acid            | Improve the bioavailability   | Anti-inflammatory, antihypertensive                                | Rotary-evaporated filmultrasonication method           | 91.76%                        | -                       | [45]      |
| Quercetin-loaded nanoparticles             | Quercetin                    | Increase antioxidant activity and release of the drug 74 times higher               | Antioxidant  | Nanoprecipitation technique                            | over 99%                      | In vitro                | [46]      |
| Breviscapine-loaded nanoparticles          | Breviscapine                 | Prolong the half-life and decrease RES uptake                                       | Cardiovascular and cerebrovascular                                 | Spontaneous emulsification solvent diffusion technique | 93.1%                         | Intra Venous            | [47]      |
| Zedoary turmeric oil nanocapsule           | Zedoary turmeric oil         | Increase the drug loading and stability of ZTO                                      | Hepatoprotection Anticancer and anti-bacterial                     | High pressure Homogenization method                    | 1.62 ± 0.15% Loading Capacity | -                       | [48]      |
| Naringenin-loaded nanoparticles            | Naringenin                   | Improved the release of NAR and improved its solubility                             | Hepatoprotective   | Nanoprecipitation method                               | -                             | Oral                    | [49]      |
| Curcuminoids solid lipid nanoparticles     | Curcuminoids                 | Prolonged-release of the curcuminoids   | Anticancer and antioxidant   | Micro-emulsion technique                               | 70%                           | In vitro                | [50]      |
| CPT-encapsulated nanoparticles             | Camptothecin                 | Prolonged blood circulation and high accumulation in tumors                         | Anticancer   | Dialysis method  | >80%                          | In vitro                | [51]      |
| <i>Ginkgo biloba</i> nanoparticles         | <i>Ginkgo biloba</i> extract | Improving the cerebral blood flow and metabolism                                    | Brain function activation  | High pressure homogenization method                    | -                             | Oral                    | [52]      |

# Fitozom

- Fitozomda; lipozomdan farklı olarak suda çözünür fito yapıların fosfolipitlerle kompleksasyonu söz konusudur. Patentli bir teknolojidir. Fosfolipidlerin hem suyu hem yağı seven yapısal özelliklerinden yararlanılarak suda çözünür maddenin lipofilik membrandan geçişi artırılmakta ve böylece biyoyararlanım artmaktadır.

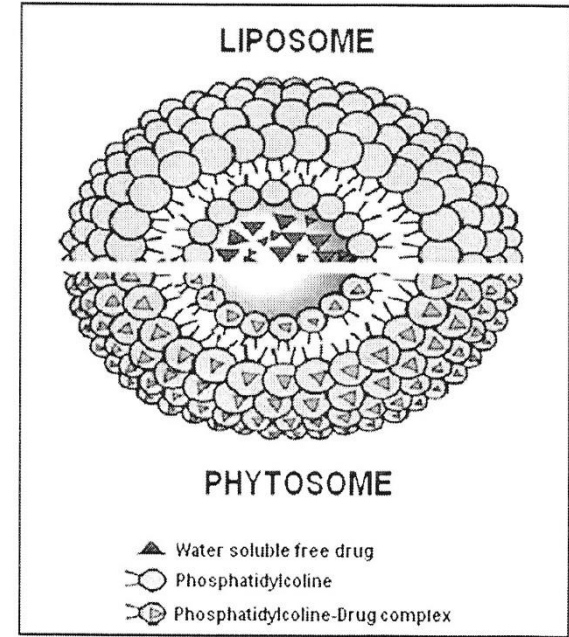


Fig. 3. Difference between liposome and phytosome [58].

**Table 3**

Phytosomal herbal formulations.

| Formulations                    | Active ingredients | Applications of phytosomal formulations  | Biological activity                              | Method of preparation               | Dose                 | Route of administration | Reference |
|---------------------------------|--------------------|--|--|-------------------------------------|----------------------|-------------------------|-----------|
| <i>Ginkgo biloba</i> phytosomes | Flavonoids         | Flavonoids of GBP stabilize the ROS  | Cardio-protective, antioxidant activity          | Phospholipids complexation          | 100 mg and 200 mg/kg | Subcutaneous            | [55]      |
| Ginkgoselect phytosome          | Flavonoids         | Inhibits lipid peroxidation (LPO), stabilize the ROS   | Hepatoprotective, antioxidant                    | Phospholipids complexation          | 25 and 50 mg/kg      | Oral                    | [56]      |
| Silybin phytosome               | Flavonoids         | Absorption of silybin phytosome from silybin is approximately seven times greater                          | Hepatoprotective, antioxidant for liver and skin | Silybin-phospholipid complexation   | 120 mg               | Oral                    | [57]      |
| Ginseng phytosome               | Ginsenosides       | Increase absorption  | Nutraceutical, immunomodulator                   | Phospholipids complexation          | 150 mg               | Oral                    | [58]      |
| Green tea phytosome             | Epigallocatechin   | Increase absorption  | Nutraceutical, systemic antioxidant, anti-cancer | Phospholipids complexation          | 50–100 mg            | Oral                    | [58]      |
| Grape seed phytosome            | Procyanidins       | The blood TRAP nTotal Radical-trapping Antioxidant Parameter) were significantly elevated over the control | Systemic antioxidant, cardio-protective          | Phospholipids complexation          | 50–100 mg            | Oral                    | [58]      |
| Hawthorn Phytosome              | Flavonoids         | Increase therapeutic efficacy and absorption   | Cardio-protective and antihypertensive           | Phospholipids Complexation          | 100 mg               | Oral                    | [58]      |
| Quercetin phytosome             | Quercetin          | Exerted better therapeutic efficacy  | Antioxidant, anticancer                          | Quercetin-phospholipid complexation | –                    | Oral                    | [59]      |
| Curcumin phytosomes             | Curcumin           | Increase antioxidant activity and Increase bioavailability   | Antioxidant, anticancer                          | Curcumin-phospholipid complexation  | 360 mg/kg            | Oral                    | [60],[49] |
| Naringenin phytosomes           | Naringenin         | Prolonged duration of action   | Antioxidant activity                             | Naringenin-phospholipid complex     | 100 mg/kg            | Oral                    | [61]      |



# Emülsiyonlar

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- Sıvı damlacıkların başka bir sıvı içinde disperse olmasıyla elde edilen sistemler.
  - Çoklu emülsiyonlar
  - Mikroemülsiyonlar

**Table 4**

Emulsion herbal formulations.

| Formulations                               | Active ingredients   | Applications of emulsion formulations   | Biological activity                            | Method of preparation               | Droplet size | Drug loading  | Route of administration | Reference |
|--|----------------------|---|--|-------------------------------------|--------------|---------------|-------------------------|-----------|
| Self-nanoemulsifying Zedoary essential oil | Zedoary turmeric oil | Improved aqueous dispersibility, stability and oral bioavailability.                | Hepatoprotection anticancer and anti-bacterial | Drawing ternary phase Diagram       | 68.3± 1.6 nm | 30%           | Oral                    | [65]      |
| Triptolide micro-emulsion                  | Triptolide           | Enhance the penetration of drugs through the stratum corneum by increased hydration | Anti-inflammatory                              | High pressure Homogenization method | <100 nm      | -             | Topical                 | [30]      |
| Docetaxel submicron emulsion               | Docetaxel            | Improve residence time  | Anticancer                                     | High pressure Homogenization method | 166.00 nm    | 90%           | Intravenous             | [66]      |
| Berberine nanoemulsion                     | Berberine            | Improve residence time and absorption   | Anticancer                                     | Drawing ternary phase diagram       | 56.80 nm     | 0.50%         | Oral                    | [67]      |
| Silybin nanoemulsion                       | Silybin              | Sustained release formulation   | Hepatoprotective                               | Emulsification method               | 21.20 nm     | -             | Intramuscular           | [68]      |
| Quercetin micro-emulsion                   | Quercetin            | Enhance penetration into stratum corneum and epidermis                              | Antioxidant                                    | High speed Homogenization method    | 10- 100 nm   | 0.3% solution | Topical                 | [69]      |

# Transferzom

Stratum corneumu geçebilen ilaç taşıyıcı sistem. Transdermal verilışte önemli.

Table 5

Other novel vesicular herbal formulations.

| Formulations                       | Active ingredients       | Applications   | Biological activity | Droplet size     | Route of administration | Reference |
|------------------------------------|--------------------------|--|---------------------|------------------|-------------------------|-----------|
| Capsaicin transferosomes           | Capsaicin                | Increase skin penetration                            | Analgesic           | 150.6 nm         | Topical                 | [71]      |
| Colchicine transferosomes          | Colchicine               | Increase skin penetration                            | Antigout            | -                | In vitro                | [77],[79] |
| Vincristine transferosomes         | Vincristine              | Increase entrapment efficiency and skin permeation y | Anticancer          | 120 nm           | In vitro                | [77]      |
| Matrine ethosome                   | Matrine                  | Improve the percutaneous permeation                  | Anti-inflammatory   | 110 ± 8 nm       | Topical                 | [76]      |
| Ammonium glycyrrhizinate ethosomes | Ammonium glycyrrhizinate | Increase of the in vitro percutaneous permeation     | Anti-inflammatory   | 350 nm to 100 nm | Topical                 | [78]      |

# Mikroküreler

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- Mikroküreler, çapları birkaç  $\mu\text{m}$  den mm boyutuna kadar değişebilen, etkin maddenin içinde homojen bir şekilde dağıtıldığı katı küresel ve monolitik matris yapıda partiküllerdir

**Table 6**

Microspheres encapsulated herbal formulations.

| Formulations                          | Active ingredients             | Applications of formulations                             | Biological activity                         | Method of preparation                   | Size in $\mu\text{m}$ | Route of administration             | Reference |
|---------------------------------------|--------------------------------|--|---|---|-----------------------|-------------------------------------|-----------|
| Rutin-alginate-chitosan microcapsules | Rutin                          | Targeting into cardiocascular and cerebrovascular region | Cardiovascular and Cerebrovascular diseases | Complex-coacervation method             | 165.00–195.00         | In vitro                            | [81]      |
| Zedoary oil microsphere               | Zedoary oil                    | Sustained release and Higher bioavailability             | Hepatoprotective                            | Quasi-emulsion-solvent diffusion method | 100–600               | Oral                                | [82]      |
| CPT loaded microspheres               | Camptothecin                   | Prolonged-release of camptothecin                        | Anticancer                                  | Oil-in-water evaporation method         | 10                    | Intraperitoneally and intravenously | [83]      |
| Quercetin microspheres                | Quercetin                      | Significantly decreases the dose size                    | Anticancer                                  | Solvent evaporation                     | 6                     | In vitro                            | [84]      |
| <i>Cynara scolymus</i> microspheres   | <i>Cynara scolymus</i> extract | Controlled release of nutraceuticals                     | Nutritional supplement                      | Spray-drying technique                  | 6–7                   | Oral                                | [85]      |

**Table 7**

Marketed novel drug delivery formulations of plant active and extracts.

| SN | Brand name   | Plant active/extracts  | Type of NDSS | Company name | Reference |
|----|--|--|--------------|--------------|-----------|
| 1  | White tea liposome Herbasec®                       | <i>Camellia sinensis</i> extract   | Liposome     | Cosmetochem  | [86]      |
| 2  | Green tea liposome Herbasec®                       | <i>Camellia sinensis</i> Extract   | Liposome     | Cosmetochem  | [86]      |
| 3  | White hibiscus liposome Herbasec®                  | White hibiscus extract   | Liposome     | Cosmetochem  | [86]      |
| 4  | Aloe vera liposome Herbasec®                       | Aloe vera Extract  | Liposome     | Cosmetochem  | [86]      |
| 5  | Guarana liposome Herbasec®                         | Guarana extract  | Liposome     | Cosmetochem  | [86]      |
| 6  | 18 $\beta$ -glycyrrhetic acid Phytosome®           | 18 $\beta$ -glycyrrhetic acid from licorice rhizome                            | Phytosome    | Indena       | [87]      |
| 7  | Centella Phytosome®                                | Triterpenes from <i>Centella asiatica</i> leaf                                 | Phytosome    | Indena       | [87]      |
| 8  | Crataegus Phytosome®                               | Vitexin-2"-O-rhamnoside from Hawthorn flower                                   | Phytosome    | Indena       | [87]      |
| 9  | Escin $\beta$ -sitosterol Phytosome®               | Escin $\beta$ -sitosterol from horse chestnut fruit                            | Phytosome    | Indena       | [87]      |
| 10 | Ginkgoselect® Phytosome®                           | Ginkgoflavonglucosides, ginkgolides, bilobalide from <i>Ginkgo biloba</i> leaf | Phytosome    | Indena       | [87]      |
| 11 | Ginselect® Phytosome®                              | Ginsenosides from <i>Panax ginseng</i> rhizome                                 | Phytosome    | Indena       | [87]      |
| 12 | <i>Ginkgo biloba</i> terpenes Phytosome®           | Ginkgolides and bilobalide from <i>Ginkgo biloba</i> leaf                      | Phytosome    | Indena       | [87]      |
| 13 | <i>Ginkgo biloba</i> dimeric flavonoids Phytosome® | Dimeric flavonoids from <i>Ginkgo biloba</i> leaf                              | Phytosome    | Indena       | [87]      |
| 14 | Greenselect® Phytosome®                            | Polyphenols from green tea leaf  | Phytosome    | Indena       | [87]      |
| 15 | Leucoselect® Phytosome®                            | Polyphenols from grape seed  | Phytosome    | Indena       | [87]      |
| 16 | Meriva®  | Curcuminoids from turmeric rhizome   | Phytosome    | Indena       | [87]      |
| 17 | PA <sub>2</sub> Phytosome®                         | Proanthocyanidin A <sub>2</sub> from horse chestnut bark                       | Phytosome    | Indena       | [87]      |
| 18 | Sericoside Phytosome®                              | Sericoside from <i>Terminalia sericea</i> bark root                            | Phytosome    | Indena       | [87]      |
| 19 | Siliphos®  | Silybin from milk thistle seed   | Phytosome    | Indena       | [87]      |
| 20 | Silymarin Phytosome®                               | Silymarin from milk thistle seed   | Phytosome    | Indena       | [87]      |
| 21 | Virtiva®   | Ginkgoflavonglucosides, ginkgolides, bilobalide from <i>Ginkgo biloba</i> leaf | Phytosome    | Indena       | [87]      |
| 22 | Visnadex®  | Visnadin from <i>Ammi visnaga</i> umbel  | Phytosome    | Indena       | [87]      |

# Kaynaklar

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