

WHAT IS CLAIMED IS:

1. A drug applicator for a system for ultrasound-enhanced delivery of at least one drug to a target site in an intraocular space, the system comprising a signal generating unit operationally connected to an ultrasound transducer,
wherein the drug applicator:
 - (a) comprises at least one space configured to hold the drug,
 - (b) is made from a low ultrasound attenuation material,
 - (c) is configured to provide low ultrasound loss coupling of the system to the sclera or cornea, and
 - (d) is configured to be mechanically coupled to the system and further configured to be coupled to the ultrasound transducer with low ultrasound loss; andwherein the signal generating unit and/or the ultrasound transducer are configured to emit an ultrasound wave form in at least one application cycle, the application cycle comprising at least one ultrasound emitting event with a time duration T_A and a waiting period with a time duration T_W .
2. A system for ultrasound-enhanced transscleral delivery of at least one drug to a target site in an intraocular space, the system comprising a signal generating unit operationally connected to an ultrasound transducer and a drug applicator,
wherein the drug applicator:
 - (a) comprises at least one space configured to hold the drug,
 - (b) is made from a low ultrasound attenuation material,
 - (c) is configured to provide low ultrasound loss coupling of the system to the sclera or cornea, and
 - (d) is configured to be mechanically coupled to the system and further configured to be coupled to the ultrasound transducer with low ultrasound loss; andwherein the signal generating unit and/or the ultrasound transducer are configured to emit an ultrasound wave form in at least one application cycle, the application cycle comprising at least one ultrasound emitting event with a time duration T_A and a waiting period with a time duration T_W .

3. The applicator according to claim 1, wherein the at least one space has at least one opening at a surface directed towards a desired site of the eye, and wherein an ultrasound coupling agent is filled in a gap between the drug applicator and the desired site of the eye.
4. The applicator according to claim 1, wherein the drug applicator is configured to be exchangeable and/or designed for a single use application.
5. The applicator according to claim 1, wherein the drug receiving space is substantially sealed at a surface designated for coupling with a desired site of the eye and the seal is configured to allow for drug permeation.
6. The applicator according to claim 1, wherein the drug receiving space is substantially open at a surface designated for coupling with the sclera.
7. The applicator according to claim 1, wherein the drug applicator is configured to be filled and/or refilled, and wherein the drug applicator receives between 10 μ L and 1.5 mL of the drug and optionally at least one additional substance.
8. The applicator according to claim 1, wherein the drug applicator is made from an elastic material having Young's Modulus of less than 10 GPa.
9. The applicator according to claim 1, wherein the drug applicator is made from at least one of the following materials:
 - epoxy resin, polyurethane rubber, polycarbonate, nylon 6 – 6, polyvinyl chloride, polyester, ultra-high molecular weight polyethylene, polypropylene, teflon, polystyrene, neoprene rubber, polyvinyl alcohol, polydimethylsiloxane, silicone-containing rubber, silicon hydrogel, silicone rubber, and
 - silicon rubber doped with at least one of the following materials: nickel, silver, palladium, tungsten, gold, platinum, silicon oxide, titanium oxide, aluminum oxide, barium sulphate, iron oxide, zirconium dioxide, cerium oxide, bismuth oxide, ytterbium oxide, lutetium oxide, hafnium oxide.
10. The applicator according to claim 1, further comprising a controller, wherein the controller is configured to control at least one of a plurality of parameters of the application cycle, the plurality parameters of the application cycle are selected from the following:

- (a) the time duration TA of the ultrasound emitting event,
- (b) the time duration TW of the wait period after the ultrasound emitting event,
- (c) the number of application cycles,
- (d) the intensity of the ultrasound emitting event,
- (e) the central frequency of the ultrasound emitting event,
- (f) the mechanical index of the ultrasound emitting system, and
in case of a pulsed ultrasound emitting event:
- (g) the repetition rate of the ultrasound emitting event and
- (h) the duty cycle of the ultrasound emitting event.

11. The applicator according to claim 1, further comprising an information receiving and/or sending unit,

wherein the information receiving and/or sending unit is configured to receive and/or send an information related to the drug; and

wherein the information receiving and/or sending unit is operationally connected to the signal generating unit and/or the controller, or wherein the information receiving and/or sending unit is operationally connected to the signal generating unit and/or the controller and the controller configured to control at least one of a plurality of parameters of the application cycle based on the information related to the drug; and

preferably the information related to the drug being stored on the drug applicator.

12. The applicator according to claim 1, wherein,

when the drug comprises molecules with a size of 70 kDa or less, the controller is configured to control the time duration TA to be between 30s and 300 s and the drug applicator is configured such that the drug transit through the sclera during the time duration TA; and/or

when the drug comprises molecules with a size of more than 70 kDa, the controller is configured to control the time duration TW to be between 60s and 600 s and the drug applicator is configured such that the molecules drug transit through the sclera during the time duration TW.

13. The applicator according to claim 1, wherein the system further comprises display and/or manual input unit configured to display and/or manually set at least one of the plurality parameters of the application cycle.

14. The applicator according to claim 1, wherein the system further comprises a temperature sensor configured to sense the temperature of the surface of the sclera or cornea, preferably a thermocouple and/or an infrared thermometer, and
- wherein the controller is configured to control the ultrasound emission event such that during the time TA the temperature of the surface of the sclera or cornea does not increase by more than 1°C.
15. A device for delivery of at least one drug to a target side in an intraocular space of an eye, wherein the device comprises:
- an ultrasound-generating device configured to generate ultrasound that is delivered to a desired site of the eye; and
- an interface configured to repeatedly couple the device to a drug applicator comprising the at least one drug, wherein the drug applicator is configured to aid in the delivery of the ultrasound to the desired site of the eye,
- wherein the interface comprises a coupling medium having a thickness that is a multiple of a propagation speed of the coupling medium over a resonance frequency.
16. The device of claim 15, wherein the coupling is effectuated without the use of a tool.
17. The device of claim 15, wherein the coupling medium has a thickness that is an odd multiple of a propagation speed of the coupling medium over four times a resonance frequency.
18. The device of claim 15, wherein the coupling medium is configured to optimize impedance matching of the ultrasound-generating device and the drug applicator.
19. The device of claim 15, wherein the coupling medium is a solid.
20. The device of claim 15, wherein the coupling medium is a liquid, suspension, or gel.
21. The device of claim 15, wherein the ultrasound-generating device is configured to be at least partially inserted into a drug applicator case, and wherein the ultrasound-generating device comprises a pin configured to slide through a slot of the case to permit the ultrasound-generating device to lock into the case.

22. The device of claim 15, wherein the drug applicator is configured to be at least partially inserted into an ultrasound-generating device case.
23. The device of claim 15, wherein the interface comprises a first fastener configured to mate with a second fastener on-board the drug applicator.
24. The device of claim 15, wherein the drug applicator has an attenuation coefficient of 5 dB/MHz/cm or lower.
25. The device of claim 15, wherein the interface provides a coupling loss of less than 10%.
26. The device of claim 15, wherein the ultrasound-generating device is configured to operate at a frequency between 20 kHz and 100 kHz.
27. The device of claim 26, wherein the ultrasound-generating device operates at an excitation voltage of less than 30 V_{RMS}.
28. The device of claim 15, wherein the ultrasound-generating device comprises a flexural transducer.
29. The device of claim 1, wherein the device is configured, with aid of the interface, to deliver ultrasound to the desired site of the eye at a mechanical index of between 0.1 and 0.3; and optionally wherein the at least one drug is delivered to the desired site of the eye at a concentration of at least 1.3 µg/ml at a speed of at least 90 µm²/s without damaging tissue of the eye.