So small and subtle – nanoparticles from solid to liquid[1]

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The ingredients of nanodispersions can partly replace pharmaceutical active agents – often with the same efficiency. Hence they are ideal base substances for cosmeceuticals.[2]

Nanodispersions, or in other words, liquids containing nano-sized particles are widely used for skin care purposes but also in dermatological cosmetics[3] and in modular form[4] for corneotherapeutic treatments.[5]
Nanodisperse lipids and oils provide excellent haptic properties. Thus, unpleasantly oily and greasing components can be transferred into sprayable aqueous lotions that penetrate into the skin within a few seconds. Water-soluble active agents, particularly those with high polarity are encapsulated into liposomes to become available for the skin; liposomes also belong to the nanodispersions.

Studies & efficacy

There is comprehensive practical experience in the context of topical-pharmaceutical and cosmetic preparations with biodegradable nanoparticles. The preparations are individually adapted to different skin conditions and skin disorders. This is the reason why no scientific studies are available. Skin tolerance and treatment results are excellent.

However, there is a multitude of studies relating to penetration features and the potential systemic toxicity of non-degradable nanoparticles as e.g. nanosilver, titanium dioxide, zinc oxide and silica, just to mention the currently most important substances. The results sometimes are ambiguous and even partially contradictory and this also applies for non-dermal preparations based on polyglycerols, polyethylene glycols and other carrier substances that are used in cancer therapy as well.

Regardless of their biodegradability and their lipophilic (oils, lipids, waxes, organic active agents), hydrophilic (liposomes with aqueous interior) or inorganic structure, nanodispersions offer high bioavailability at low doses of active agents.[6] The irritation threshold - based on the formation of vitamin A acid - for liquid, retinyl palmitate (vitamin A) laden nanoparticles is lower than for conventional emulsions.[7] Liposomes with sodium ascorbyl phosphate (vitamin C) already inhibit melanin formation in very low concentration.[8]

Without additives

Other than conventional formulations, nanodispersions, or in other words, preparations with particles smaller than 1 µm (= 1000 nm), allow a reduction or even elimination of additives such as emulsifiers, spreading substances and penetration enhancers. Additives often stress the skin and even can be counterproductive when they encourage wash-out effects or irritations. On top of that, a combination

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[1] H. Lautenschläger, Indikationsgemäße Anwendungen von Nanodispersionen, Vortrag auf der 19. Jahrestagung der Gesellschaft für Dermopharmazie (GD) in Berlin am 18.3.2015
[2] H. Lautenschläger, Cosmeceuticals, medical Beauty Forum 2014 (4), 16-18
[3] H. Lautenschläger, Dermatologische Kosmetik – Brücke zwischen Kosmetik und Medizin, Kosmetische Praxis 2005 (5), 12-14
[4] H. Lautenschläger, Mikrokosmos modularer dermaler Zusammensetzungen, Vortrag auf der 18. Jahrestagung der Gesellschaft für Dermopharmazie (GD) in Berlin am 9.4.2014
[5] H. Lautenschläger, Geschichte und aktuelle Gesichtspunkte der Korneotherapie, Kosmetische Medizin 26 (2), 58-60 (2005)
[6] H. Lautenschläger, Nanopartikel in Kosmetika – gut oder schlecht? Beauty Forum 2009 (5), 44-47
[7] Cosmetics & Toiletries 119 (6), 68 (2004)
[8] H. Lautenschläger, Hautaufhellende Wirkstoffe von A-Z – ein Überblick, Kosmetik International 2013 (9), 22-28

of nanodispersions with conventional formulations usually fails because of the incompatibility of emulsifiers.[9]
Since the risk of sensitizations increases with permeation of the preservatives listed in the annex of the EU Cosmetic Directive, nanodispersions, without exception, are produced in a sterile form (ampoules) or without preservatives. The advantage thereof: the focus now is on physiological concepts.

Degradable or non-degradable?

A distinction is made between solid and liquid nanoparticles. Their degradability depends on the individual components that were processed.

- Solid nanoparticles, with exception of the organic nanocrystals, mostly either are non-degradable or rather persistent to degradation. The most important variants are:
  - Nanocrystals of difficultly soluble organic substances or organic substances with high-melting-point such as boswellia acids (frankincense), phytosterines, flavonoids and their glycosides such as for instance rutin, as well as ceramides.
  - Lipid nanoparticles made of waxes, poly-alpha-olefins and other hydrocarbons. They coalesce on the skin to form occlusive films from which then lipophilic active agents such as coenzyme Q_{10} are released.
  - Polymer beads made of polyamides, polypeptides or polysaccharides with embedded, mostly pharmaceutical active agents.
  - Silica-nanoparticles (silicic acid), which integrate and stabilize amorphous active agents and pigments in their pores.
  - Inorganic substances such as titanium dioxide, zinc oxide and carbon (carbon black) for sun protection purposes or decorative cosmetics.
  - Elementary precious metals such as silver and gold. Gold forms red dispersions; silver has antibacterial and anti-inflammatory properties.
- Liquid nanoparticles based on phosphatidylcholine are easily biodegradable. Penetrating into the skin are the molecular individual components but not the entire particles. They include:
  - Nanoparticles with fat-soluble active agents such as vitamins, coenzyme Q_{10}, ceramides, vegetable oils and essential fatty acids.
  - Liposomes with water-soluble vitamins, antioxidants, glycosides, moisturizers etc.

Nanodispersions with small particles look like aqueous solutions while particles larger than 400 nm result in an opaque or even milky consistency. They can also be coloured such as for instance gold dispersions.

Cosmetic applications

Applications in dermatological cosmetics are the supportive prevention and the adjuvant skin care[10] in the case of skin problems. In this context, individual substances as well as mixtures of substances and herbal extracts are used. The emphasis is on biodegradable nanodispersions that are compatible with the human physiology.[11] Particularly the skin care at barrier-, cornification- and connective tissue disorders plays an important role. Examples are neurodermatitis,[12] perioral dermatitis,[13] psoriasis,[14] acne[15] and rosacea.[16]

[9] H. Lautenschläger, Huckepack – Übersicht Trägersysteme, medical Beauty Forum 2013 (1), 16-18
[10] H. Lautenschläger, Nutzen von lamellaren Präparaten in der Hautpflege, im Hautschutz und in der dermatologischen Therapie, Vortrag auf der 17. Jahrestagung der Gesellschaft für Dermopharmazie (GD) in Mainz am 23.3.2013
[11] H. Lautenschläger, Biodegradable lamellar systems in skin care, skin protection and dermatology, SOFW-Journal 139 (8), 2-8 (2013)
[12] H. Lautenschläger, Pflege bei Neurodermitis – Die Barriere unterstützen, Kosmetische Praxis 2005 (1), 9-11
[13] H. Lautenschläger, Lippenerkenntnisse – Bewährte und neue Pflegetipps, medical Beauty Forum 2014 (6), 18-20
[14] H. Lautenschläger, Hautpflege bei Schuppenflechte – ganz individuell, Beauty Forum 2009 (10), 48-51
[15] H. Lautenschläger, Akne: Möglichkeiten der kosmetischen Prävention, Beauty Forum 2015 (2), 88-91
[16] H. Lautenschläger, Korneotherapeutische Hautpflege bei Rosacea, Ästhetische Dermatologie (mdm) 2010 (3), 16-20

The prevention and treatment of hyperpigmentations,[17] premature skin aging ("anti-aging“) as well as the skin care of sun and radiation stressed skin are additional fields of application.

Chart: Frequently used active agents
Liposomes (L); liquid (N), solid (SN) nanoparticles; biodegradable (+), non-degradable (-)

Active agent	Carrier	Application	Mechanism of action
aescin	L+	rosacea couperosis	vascular permeability ↓, oedema↓
amino acids	L+	dry skin	moisturizers, radical scavengers
azelaic acid	L+	acne, rosacea, perioral dermatitis (POD)	5-α-reductase-inhibition
boswellic acids	L+, N+, SN+	acne, POD, rosacea, neurodermatitis, erythema	protease inhibition, 5-lipoxygenase-inhibition
butcher’s broom extract	L+, N+	rosacea couperosis	vascular permeability ↓, oedema↓
caffeine	L+	microcirculation, cellulite	peripheral vasodilatation, lipolysis
carbon black	SN-	make-up	pigment
ceramide	SN+	skin protection	TEWL ↓
coenzyme Q_{10}	N+, SN-	anti-aging	metabolism ↑
eyebright	L+	eye care	unknown
fumaric acid	L+	psoriasis	collagen metabolism ↑?
grape seed extract	L+	anti-aging	radical scavenger (OPC)
isoflavones	L+	oestrogen effects	phytohormones
kigelia extract	L+	rosacea couperosis	vascular permeability ↓, oedema↓
niacinamide	L+	acne, bad skin, recovery	vitamin B_3
oils with bound linoleic acid	N+	barrier disorders, erythema	ceramide substrate, metabolisation through 15-lipoxygenase (LOX)
oils with bound α-linolenic acid	N+	erythema	metabolisation through 15-LOX
oils with bound γ-linolenic acid	N+	neurodermatitis, erythema	δ-desaturase defect, metabolisation through 15-LOX
phosphatidylcholine	L+, N+	acne, barrier-, cornification disorders	ceramide substrate, metabolisation through 15-LOX
retinol palmitate	N+	acne, scars, recovery	vitamin A

[17] H. Lautenschläger, Haut ohne Makel – Wirkstoffe und Wirkstoffsysteme, medical Beauty Forum 2014 (5), 32-35

Active agent	Carrier	Application	Mechanism of action
rutin	SN+	rosacea couperosis	vascular permeability↓, oedema↓
silica	SN-	make-up	pigment
silver	SN-	inflammations	antibacterial
sodium ascorbyl phosphate	L+	hyperpigmentation, laser	vitamin C, tyrosinase inhibition
spilanthol	L+	wrinkle reduction	muscle relaxation
titanium dioxide	SN-	light protection, make-up	UV filter, pigment
tocopherol acetate	N+	skin protection	vitamin E
tranexamic acid	L+	hyperpigmentation, rosacea	tyrosinase inhibition, vascular permeability ↓
various herbal extracts	L+	hyperpigmentation, laser	tyrosinase inhibition
zinc oxide	SN+	light protection	UV filter
zinc salts	L+	acne, bad skin	superoxide dismutase (SOD) substrate

According to regulation EC1223/2009 of the EU Cosmetic Directive applicable as of 11.07.2013, nanoparticles of the size of 100 nm or smaller have to be declared as nanomaterial. They are subject to severe restrictions. Exempt from the regulation are liquid, biodegradable nanoparticles that in the skin barrier already decompose into their individual components.

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