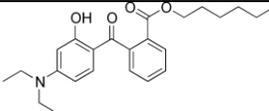
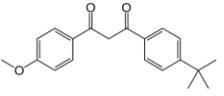
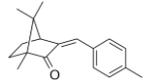
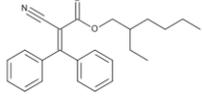
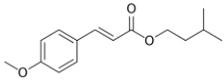
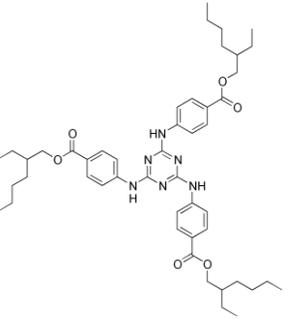
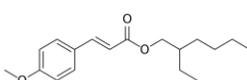
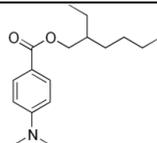
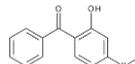
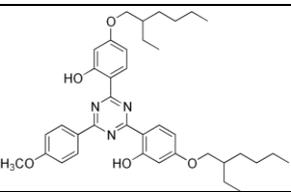
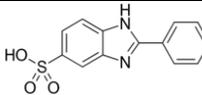


Table 1 - Experimental and predicted physical-chemical parameters of the most recently investigated UV-absorbers.

INCI name (INN/XAN)	Chemical structure	Brand name	Absorption spectrum range	Molecular weight (g/mol) <sup>4</sup>	LogP	Water solubility (mg/L)	Melting point (°C)
diethylamino hydroxybenzoyl hexyl benzoate		Uvinul <sup>®</sup> A Plus	UVA1	397.515	5.7-6.2 <sup>1</sup>	<0.01 (20°C) <sup>1</sup>	54; 314 (dec.) <sup>1</sup>
Butyl methoxydibenzoylmethane (avobenzene)		Eusolex <sup>®</sup> 9020, Parsol <sup>®</sup> 1789	UVA	310.393	4.51 <sup>4</sup>	2.2 (25°C) <sup>4</sup>	83.5 <sup>4</sup>
4-methylbenzylidene camphor (enzacamene)		Eusolex <sup>®</sup> 6300 Parsol <sup>®</sup> 5000 Uvinul <sup>®</sup> MBC 95	UVB	258.397	4.95	1.3 (20°C)	66–68
Octocrylene (octocrilene)		Eusolex <sup>®</sup> OCR, Parsol <sup>®</sup> 340, Uvinul <sup>®</sup> N539T, NeoHeliopan <sup>®</sup> 303 USP	UVB	361.485	6.78 <sup>3</sup>	0.0038 <sup>3</sup>	N/A
isoamyl p-methoxycinnamate (amiloxate)		Neo Heliopan <sup>®</sup> E1000	UVB	248.322	3.6 <sup>1</sup>	4.9 (25°C) <sup>1</sup>	N/A
Ethylhexyl triazone		Uvinul <sup>®</sup> T150	UVB	823.092	> 7(20 °C) <sup>6</sup>	< 0.001 (20.0 °C) <sup>6</sup>	129 <sup>6</sup>

Ethylhexyl methoxycinnamate (octinoxate)		Parsol <sup>®</sup> MCX, Heliopan <sup>®</sup> New	UVB	290.403	6.1 <sup>4</sup>	0.041 (24 °C and pH 7.1) <sup>4</sup>	N/A
Ethylhexyl dimethyl PABA (padimate-O)		Escalol <sup>™</sup> 507 Arlatone 507 Eusolex 6007	UVB	277.408 <sup>4</sup>	5.77 <sup>4</sup>	0.54 (25 °C) <sup>4</sup>	N/A
benzophenone-3 (oxybenzone)		Eusolex <sup>®</sup> 4360	UVA2+ UVB	228.247	3.7 <sup>2</sup>	3.7 (20°C) <sup>2</sup>	62-65 <sup>2</sup>
bis-ethylhexyloxyphenol methoxyphenol triazine (bemotrizinol)		Tinosorb <sup>®</sup> S	UVA1+UVB	627.826	12.6 <sup>1</sup>	<10 <sup>-4</sup>	80.40 <sup>1</sup>
Phenylbenzimidazole sulfonic acid (ensulizole)		Eusolex <sup>®</sup> 232 Parsol <sup>®</sup> HS Neo Heliopan <sup>®</sup> Hydro	UVA2+ UVB	274.294 <sup>5</sup>	-1.1 (pH 5) -2.1 (pH 8) <sup>5</sup>	> 30% (As sodium or triethanolammonium salt at 20°C) <sup>5</sup>	N/A

<sup>1</sup> (3)

<sup>2</sup> (34)

<sup>3</sup> (44)

<sup>4</sup> Pubchem

<sup>5</sup> SCCP/1056/06 Opinion on phenylbenzimidazole sulfonic acid and its salts

<sup>6</sup> BASF safety data sheet

Table 2 – In vitro studies for the assessment of skin permeation/penetration of sunscreens.

Reference	Sun-filter (INCI name)	Formulation	Substrate	Equipment	T (°C)	Receiving phase	Lenght (h)	Analitycal procedure	Results
(3)	Isoamyl p-methoxycinnamate, IPMC - Diethylamino hydroxybenzoyl hexyl benzoate, DHHB - Bis-ethylhexyloxyphenol methoxyphenol triazine, BMZ	Biomimetic O/W cream	Full thickness (1mm) porcine ear skin	Franz cell	30	6% Brij PBS	12	HPLC - receiving phase withdrawn after 12h -SC 15 tape strips -remaining tissue	None of the molecules was detected in the receiving phase after 12h and the sunscreens were largely detected in the 5 tape strips
(5)	Benzophenone-3, BP-3	SLM	Porcine ear skin	Franz cell	37	Buffer 150 mM pH7.2 + 0.5% Tween 80	12	tape stripping (SC) and E+D	SLM with natural waxes are able to inhibit permeation and reduce 3-fold penetration with respect to free B3
(6)	Benzophenone-3, BP3	- Emulsion - Emulsion with BP3 encapsulated in mesoporous silica	Cellulose membrane	Franz cell	37	pH 7.4 buffer + 2% tween 20	24	UVvis	Skin permeation of BP3 was prevented due to encapsulation by MS
(7)	- Bis-ethylhexyloxyphenol methoxyphenol triazine, BMZ - Ethylhexyl triazone, ETZ - Diethylamino hydroxybenzoyl hexyl benzoate, DHHB - Ethylhexyl methoxycinnamate, OMC - Butyl methoxydibenzoylmetha	NLC	Human skin (SC+E separated from the dermis by treatment at 60°C for 2 min.)	Franz cell	32	EtOH/water 50:50	24		Comparison NLC/nanoemulsion; NLC reduce permeation and the filter remains on the skin surface

	ne, AVO								
(9)	4-methylbenzylidene camphor, 4-MBC	- 4-MBC polymeric microsphere formulated in O/W emulsion - free 4-MBC in O/W emulsion	Episkin	Harvard apparatus	37	pH 7.4 phosphate buffer 66.7mM + 1% Brij98	5	HPLC tape stripping (2 strips for SC) extraction from remaining E	Encapsulation in microspheres remarkably reduced the permeation of 4-MBC and increased its retention on the skin surface
(13)	- Benzophenone-3, BP3 - Butyl methoxydibenzoylmethane, AVO - Zinc oxide, ZnO	EtOH/buffer	Nude mice - 8 and 24 weeks	Franz cell	37	30% EtOH/pH 7.4 buffer	24	- HPLC - atomic abs. differential stripping (20 strips and cyan.)	UVA and UVA/UVB increase follicular uptake for BP-3 and AVO, particularly for senescent skin; ZnO no permeation/penetration; AVO no permeation and penetration higher for young skin
(14)	Ethylhexyl dimethyl PABA	Bioadhesive nanoparticles (BNP)	Fresh pig skin	Incubation of skin with formulation in humidity chamber and subsequent washing with PBS buffer	32	/	6	HPLC tape stripping 30 times, remaining skin chopped and extraction performed	No PO penetrated in the skin from PO/BNPs; minimal amounts were found in the tape stripped skin, suggesting minimal epidermal penetration
(16)	- Bis-ethylhexyloxyphenol methoxyphenol triazine (BMZ) - Ethylhexyl methoxycinnamate, OMC - Butyl methoxydibenzoylmethane, AVO - Octocrylene, OCT	O/W Emulsion	Porcine ear skin dermatomed at 500 $\mu$ m	Franz cell	32	Phosphate buffer (pH 7.4 - 0.1M) + 4% w/v BSA	12	HPLC tape stripping (16 strips) and E+D cut in little pieces	The permeated amounts were below LLOQ; over 90% was retained in the SC; the presence of both resveratrol and carotene reduced the amount of UV filters in the SC; BMZ exhibited the lowest penetration rate

	- Resveratrol □□β-Carotene								
(34)	Benzophenone-3, BP3	SLN NLC NPLC NC	Porcine ear skin dermatomed at 600 μm	Franz cell	37	Albumina PBS solution	24	HPLC - SC: 20 tape strips -E and D separated with scalpel	NPLC and NC were able to significantly reduce BP-3 flux across the skin, exhibiting high in vitro SPF
(35)	- Butyl methoxydibenzoylmeta ne, AVO - Benzophenone-3, BP-3 - Phenylbenzimidazole sulfonic acid, ESZ	Complex with β-cyclodextrin o/w cream	Wistar male rats abdominal skin	Franz cell	37	phosphate buffer 7.4 and isopropyl alcohol 70:30	6	HPLC	ESZ permeated the rat skin in a higher amount; the complex BP-3-CD was found to be the safest one, both in terms of slow rate of permeation and prolonged lag-time
(41)	Butyl methoxydibenzoylmeta ne, AVO	- AVO encapsulated in modified dextrin formulated in O/W emulsion - free AVO in O/W emulsion	Cellulose membrane	Franz cell	37	pH 5.5 buffer + 2% tween 20	6		Avobenzone encapsulated in modified dextrin and dispersed in an emulsion exhibited a transdermal flux 2.5-fold lower than free avobenzone.