

Supplementary Materials:

Stability and Safety Traits of Novel Cyclosporine A and Tacrolimus Ophthalmic Galenic Formulations Involved in Vernal Keratoconjunctivitis Treatment by a High-Resolution Mass Spectrometry Approach

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Table S1. Research studies collection on Cyclosporine A and Tacrolimus based ophthalmic formulations for Vernal keratoconjunctivitis treatments.

Author	years	Active compound concentration	Formulation type	Pathology	Treatment/experiment duration	Results
Cyclosporine based formulations						
Clinical trial						
BenEzra	1986	2%	Lacrimart	VKC	6 weeks	Signs and symptoms improvement after the first week of treatment.
Secchi	1990	2%	oil	VKC	4–9 months	Within the first 15 days, both symptoms and signs of the condition improved significantly.
Pucci	2002	2%	oil	VKC	4 times a day for 4 months	Signs and symptoms improvement after two weeks of treatment.
Akpek	2004	0.05%	Lacrimart	AKC	4–6 times a day for 1 month	Signs and symptoms improvement after one month of treatment.
Kilic	2006	2%	Lacrimart	VKC	5 times a day for 14 weeks	Signs and symptoms improvement after two weeks of treatment.
Spadavecchia	2006	1% and 1.25%	Lacrimart	VKC	4 times a day for 4 months	Signs and symptoms improvement after two weeks of treatment in both groups.
Oczan	2007	0.05%	Lacrimart	VKC, AKC	2–4 times a day for 6 months	Signs and symptoms improvement after six months of treatment.
Pucci	2010	1–2%	Lacrimart	VKC	2–4 times a day for 2–7 years	Signs improvement during the study

Lambiase	2011	0.05% and 0.025%	oil	VKC	2 times a day for 6 months	Signs and symptoms improvement during the study period.
Takamura	2011	0.1%	Lacrimart	VKC	6 months	Signs and symptoms improvement after six months of treatment.
Keklicki	2014	0.05%	Lacrimart	VKC	4 times a day for 4 weeks	Signs and symptoms improvement after one month of treatment.
Yucel	2016	0.05%	Lacrimart	VKC	4 times a day for 3 months	Signs and symptoms improvement after one month of treatment.
Leonardi	2019	0.1%	Cationic emulsion	VKC	2–4 times a day for 4 months	Signs and symptoms improvement after four months of treatment.
Compositional/stability studies						
Chennell	2017	1–2%	Micellar solution	In vitro	-	The micellar formulation can be stored at 5 °C or at ≤25 °C for up to 6 months.
Lallemand	2017	variable	Lacrimart, oil	VKC, dry eye	variable	Restasis and Ikervis are the two major and successful emulsion products
Shen	2018	variable	mPEG-PLA polymer micelles	Human corneal epithelial and rabbits.	-	mPEG-PLA diblock polymer can be potentially used as a nanoscopic carrier to deliver hydrophobic drugs to the ocular region
Tacrolimus based formulations						
Clinical trials						
Vichyanond	2004	0.1%	ointment	VKC	1–2 times a day for 1 month	Signs and symptoms improvement after one month of treatment.
Miyazaki	2008	0.02%	ointment	VKC, AKC	1–4 times a day for 26 months	Signs improvement during the study period.
Ohashi	2010	0.1%	Lacrimart	VKC, AKC	2 times a day for 1 month	Signs and symptoms improvement after one month of treatment.
Kheirkhah	2011	0.005%	Lacrimart	VKC	4 times a day for 10 months	Signs and symptoms improvement during the study period.
Labcharoenwongs	2012	0.1%	ointment	VKC	2 times a day for 2 months	Signs and symptoms improvement after one month of treatment.
Fukushima	2014	0.1%	Lacrimart	VKC, AKC	2 times a day for 6 months	Signs and symptoms improvement after one month of treatment.
Pucci	2015	0.1%	Lacrimart	VKC	3 times a day for 3 weeks	Signs and symptoms improvement after three weeks of treatment.
Al-Amri	2016	0.1%	ointment	VKC	Variable	Signs and symptoms improvement after six weeks of treatment.
Chatterjee	2016	0.03%	ointment	VKC	3 times a day for 3 months	Signs and symptoms improvement after four weeks of treatment.
Barot	2016	0.1%	ointment	VKC, AKC	2 times a day for 3 months	Signs and symptoms improvement after four weeks of treatment.

Miyazaki ²	2017	0.1%	Lacrimart	VKC, AKC	2 times a day for 3 months	Signs improvement after three months of treatment.
Compositional/stability studies						
Zeng	2016	0.1%	Niosomes and mucoadhesive hyaluronic acid	rabbits	-	The hybrid system facilitated FK506 ocular delivery on mucoadhesion, precorneal retention, aqueous humor pharmacokinetics and transcorneal permeability
Ezquer-Garin	2017	0.03%	Lacrimart	In vitro	-	Tacrolimus in eye drop solution was stable for 20 days when stored at 25 °C and for at least 85 days when stored at 2–8 °C or between –15 and –25 °C
Luaces-Rodríguez	2018	0.03%	BBS (Balanced Salt Solution), PVA (Polyvinyl alcohol) and Hyaluronic Acid	Rats, VKC, AKC	6 months	Formulations with PVA and Hyaluronic Acid present more retention time on the ocular surface of rats than PBS



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