Efficacy and safety of an antiviral Iota-Carrageenan nasal spray: a randomized, double-blind, placebo-controlled pilot study in volunteers with early symptoms of the common cold

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Background: The common cold, the most prevalent contagious viral disease in humans still lacks a safe and effective antiviral treatment. Iota-Carrageenan is broadly active against respiratory viruses in-vitro and has an excellent safety profile. This study investigated the efficacy and safety of an Iota-Carrageenan nasal spray in patients with common cold symptoms.

Results: In a randomized, double-blind, placebo-controlled pilot trial, 35 human subjects suffering from early symptoms of common cold received Iota-Carrageenan (0,12%), a biopolymer isolated from red seaweed, in a saline solution three times daily for 4 days, compared to placebo. Administration of Iota-Carrageenan nasal spray reduced the symptoms of common cold (p=0,046) and the viral load in nasal lavages (p=0,009) in patients with early symptoms of common cold. Pro-inflammatory mediators FGF-2, Fractalkine, GRO, G-CSF, IL-8, IL-1β, IP-10, IL-10, and INF-α2 were reduced in the Iota-Carrageenan group.

Conclusion: Iota-Carrageenan nasal spray appears to be promising for safe and effective treatment of early symptoms of common cold. Larger trials are indicated to confirm the results.

Iota-carrageenan inhibits replication of HRV serotypes 1A, 8, 14, 16 and 83 on primary human epithelial cells (1)

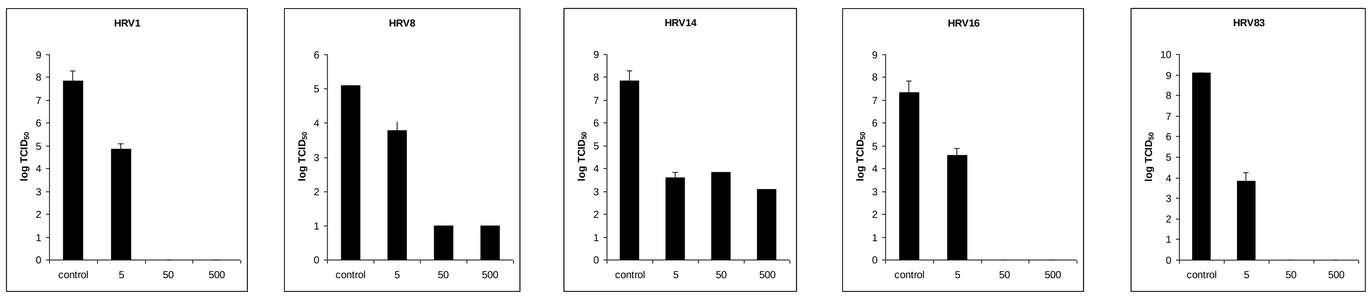
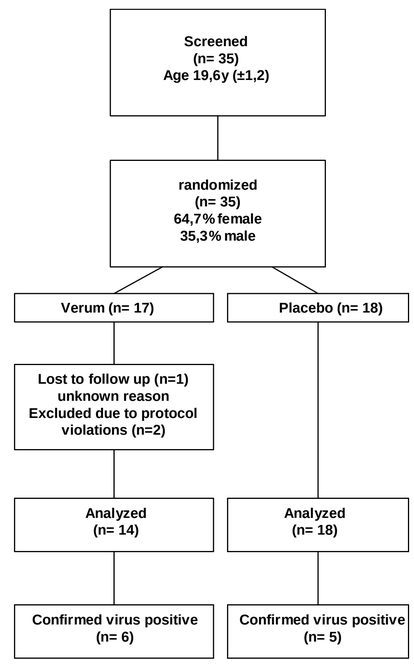


Figure 1
Effect of Iota carageenan on the replication of HRV strains 1A, 8, 14, 16 and 83 on human nasal epithelial cells.
HNep cells were infected with different HRV strains (indicated at the top of each panel; 0,1 $TCID_{50}$/cell) in the presence of Iota-Carrageenan at the concentrations indicated at the x-axis. 30 minutes after infection the inoculum was removed and medium containing Iota-Carrageenan was added. Viral titers in the supernatants of infected cells were determined after 48 h by $TCID_{50}$ assay on HeLa cells (y-axis). Bars represent means from four parallel experiments, standard deviations are indicated.

Flow chart of clinical trial



Efficacy of the Iota-Carrageenan nasal spray

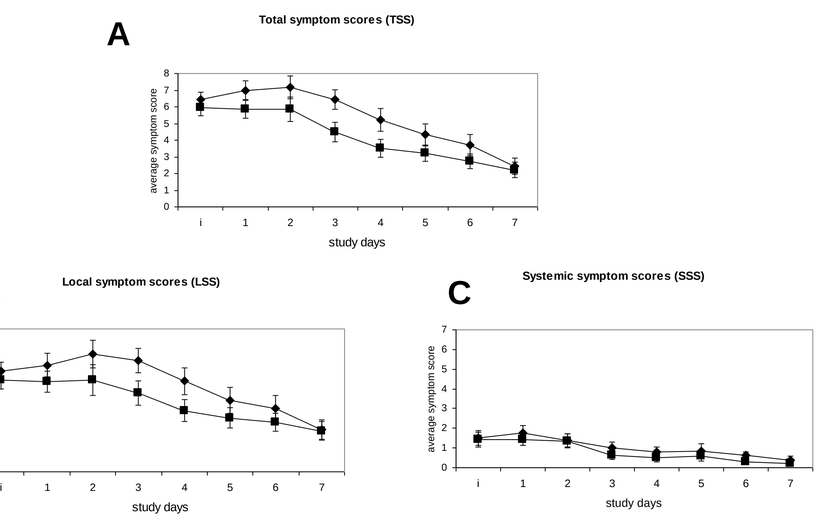


Figure 3 Mean symptom scores over 7 days
Mean ± SEM for Carrageenan nasal spray (black squares) and Placebo (black triangles) treatment groups. A. Total symptom scores B. Local Symptom scores C. Systemic symptom scores. The y axis shows the study day; i indicates the point of inclusion into the study**.**

Figure 4 Red seaweed

Virus analysis of nasal lavages

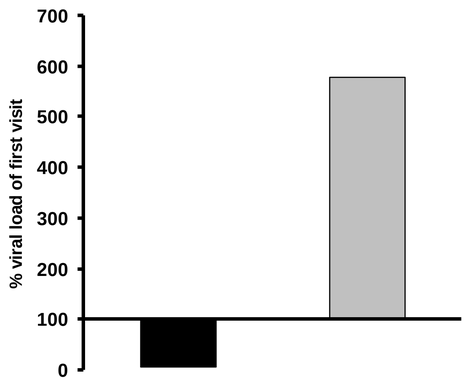


Figure 5 Relative viral load at day 3/4 in % of day 1
Shown is the relative viral load on day 3/4 in percent of the viral load on day 1.The cT values of all positive samples were anti-logged on the basis of 2. The resulting values of virus positive samples from the first visit were set 100%. The relative quantity of virus positive samples at the second visit was calculated in percent of the value of the first visit. The cT numbers of Verum and placebo samples of day 1 and day 3/4 were compared by applying a Mann-Whitney U-test (p=0,009). The black bar shows verum (0,12% Iota-Carrageenan) and the grey bar shows placebo (NaCl).

Efficacy on individual symptoms

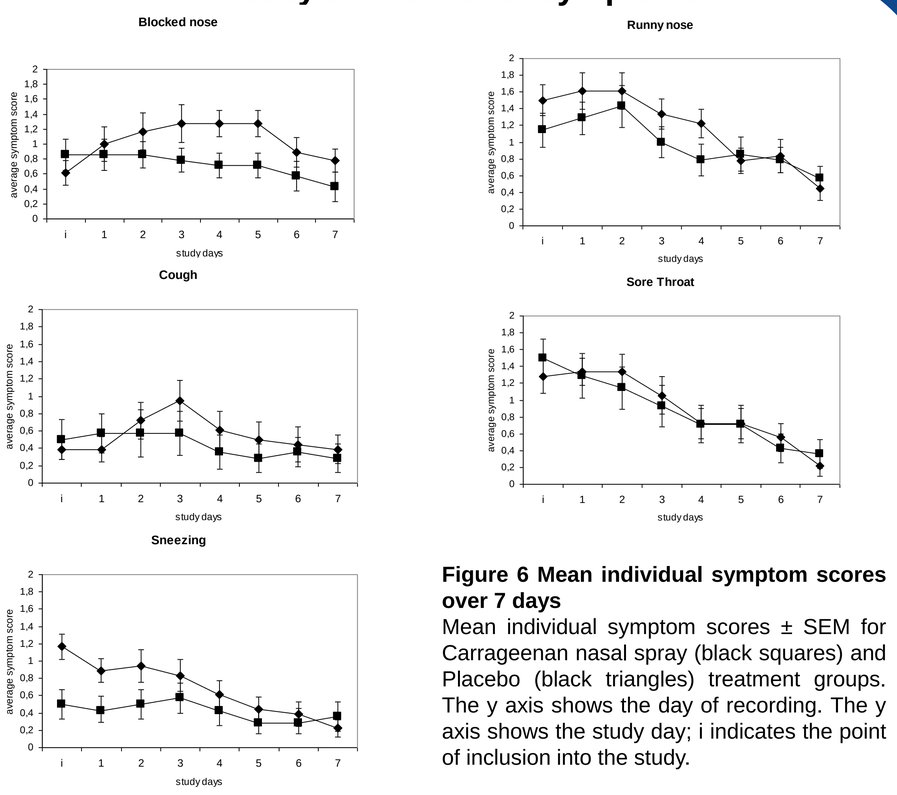


Figure 6 Mean individual symptom scores over 7 days
Mean individual symptom scores ± SEM for Carrageenan nasal spray (black squares) and Placebo (black triangles) treatment groups. The y axis shows the day of recording. The y axis shows the study day; i indicates the point of inclusion into the study.

Analysis of cytokines in nasal lavages

	first visit day 1	second visit day 3/4	second visit day 3/4	
	all	Verum	Placebo	p-value
FGF-2	5,9 (5,9)	2,5 (2,8)	7,5 (5,6)	0,04
Fraktalkine	87,0 (74,5)	46,4 (32,4)	79,7 (39,3)	0,023
GRO	252 (233)	156 (112)	339 (417)	n.s.
G-CSF	45,5 (89,1)	10,9 (17,9)	78,5 (186)	n.s.
IL-8	18,7 (30,6)	14,4 (10,8)	21,0 (22,4)	n.s.
IL-1α	35,3 (30,0)	28,8 (14,4)	43,1 (28,9)	n.s.
IP-10	1790 (3177)	970 (1769)	3016 (4033)	n.s.
IL-10	1,6 (4,22)	0 (0)	5,5 (13,6)	0,049
IL-1ra	164 (129)	174 (320)	131 (85)	n.s.
INF-α2	11,6 (8,0)	8,7 (4,1)	11,5 (5,6)	n.s.
IL-12(p40)	10,6 (14,0)	9,1 (9,7)	8,0 (9,8)	n.s.

Figure 7 Comparison of cytokine levels on day 1 and day 3/4. Shown are mean levels in pg/ml ± standard deviation. Lower quantification limit was 3.2 pg/ ml, values below were set to `0´. P-values: comparison verum versus placebo by Mann-Whitney U-test. Cytokine concentration was determined by Milliplex MAP Human Cytokine/ Chemokine Kit 96 Well Plate Assay (Millipore Corp., St. Charles, USA) according to the manufacturer's instruction.

Treatment with Iota-Carrageenan nasal spray was superior to placebo (p=0,046) with respect to the primary endpoint mean of TSS over days 2-4 (2)

End point	Carrageenan nasal spray n=14	Placebo nasal spray n=18	p-value
Primary endpoint			
TSS mean of sum on days 2-4	4,62 ± 2,06	6,28 ± 2,29	0,046
Secondary endpoints			
LSS mean of sum on days 2-4	3,79 ± 2,03	5,22 ± 2,30	0,068
SSS mean of sum on days 2-4	0,83 ± 0,75	1,06 ± 1,07	0,704

Figure 8 The primary efficacy parameter for the trial was the difference between verum and placebo in total symptom scores on days 2-4 (TSS 2-4).

Conclusion:

Iota-Carrageenan nasal spray appears to be a promising compound for safe and effective treatment of early symptoms of common cold. Larger clinical trials are needed to study the therapeutic index in more detail.

Reference: 1. Grassauer A, Weinmuellner R, Meier C, Prieschl-Grassauer E, Unger H; *Virology Journal* 2008, **5:**107
2. Eccles R, Meier C, Jawad M, Weinmüllner R, Grassauer A, Prieschl-Grassauer E; Respir Res. 2010 Aug 10;11:108.