Lonza

Galactoarabinan as a Multi-functional, Natural Enhancer for Skin Care Actives and Personal Care Formulations.

LaraCare® A200, galactoarabinan (GA) is a multi-functional polysaccharide that is extracted from the already-harvested North American Larch tree which grows in abundance in the Northwestern United States. It is an all-natural, water-dispersible polymer which functions as an enhancer for skin care actives and personal care formulations.

Larch Tree Background[1] and Its Uses

Larch pines trees, found mostly in the cold latitudes, grow at elevations over 2,000 feet on open mountain slopes. In the United States, Galactoarabinan can be sourced from either the Western Larch or the Tamarac tree, since GA is equivalent across the two species. These trees differ in the non-GA portion of the tree. However, it is the Tamarac tree that is used as the predominant source of LaraCare® A200.

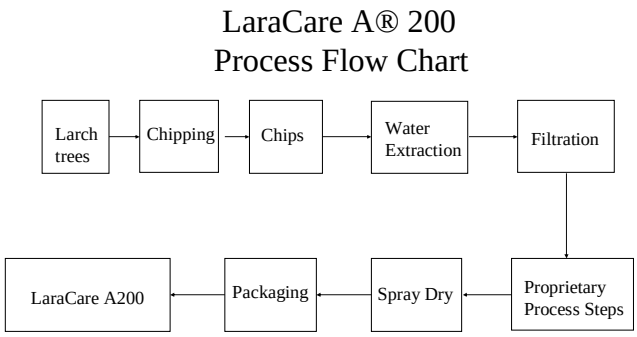
For good forestry practices, the U.S. Government mandates that a certain population of trees be harvested every year. In Minnesota, the Tamarac tree grows in the midst of these harvested resources. The harvest is sustainable, as only 1% is taken—never to deplete the population. This required 1% harvest provides ample supply of raw materials for production of LaraCare® A200. GA is extracted from the heartwood of the tree; it is not found in the bark. Since it originates in the non-living portion of the tree, it is not susceptible to disease, nor depends on the nutrients absorbed from the soil.

The western larch trees are typically cultivated for their timber. These trees also have a dark brown resinous material exuded from their bark which is a main source of galactoarabinan. According to folklore, early U.S. inhabitants have used the resin, leaves and bark of the western larch for food, cosmetic and medicinal applications. The Thompson Indians prepared a mixture of the GA resin with fat for use as an application for sores, cuts and burns [1].

Extraction Technology[1]

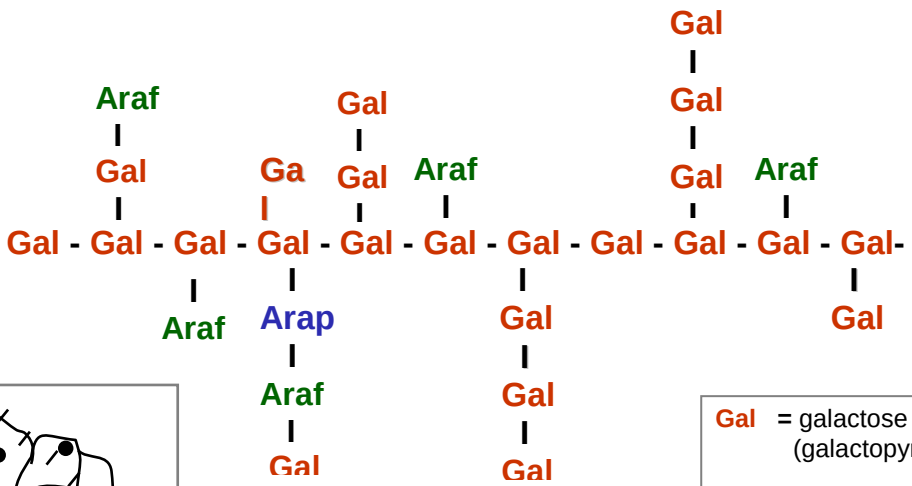
Typical western larch trees and Tamarac trees contain approximately 15% and 8% galactorarabinan, respectively, but may contain up to about 23%. Older trees may provide higher yields. Galactoarabinan is found in the interior of the plant cell. GA is not part of the plant cell wall, which would make it more difficult to extract. The patented and proprietary process is a water-based extraction using only heat, pressure and water, without using any organic solvents. The general process schematic is given below in Figure 1. The waste from the extraction process is used for making composite board and fiber matting.

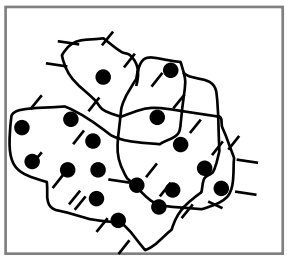
Figure 1.



Galactoarabinan is natural, branched polysaccharide composed of beta-linked galactose units with side chains of galactose and arabinose. Galactose and arabinose are present in a ratio of 6:1, respectively. Its structure is given below in Figure 2.

Figure 2. Chemical Structure of Galactoarabinan





Spherical Globular Structure in Water

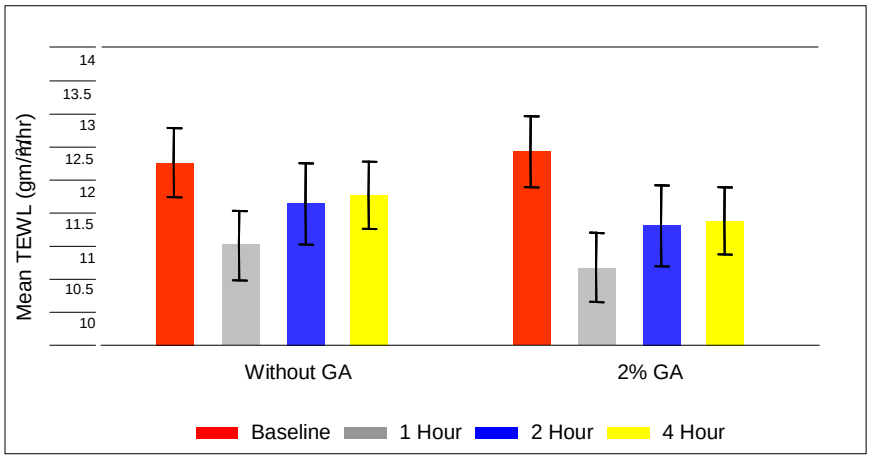
Key Technical Effects
Incorporation of LaraCare® A200 into personal care formulations has enhanced various desirable skin effects such as TEWL reduction and reduction of the appearance of fine lines and wrinkles [2]. In addition, LaraCare® A200 has also been seen to facilitate a generally smaller droplet size in oil-in-water emulsions, as well as improve dispersion of particulates such as inorganic sunscreens in personal care formulations. These particular attributes seem to have enabled SPF enhancement of some typical sunscreen actives [2].

Reduction of TEWL
Transepidermal Water Loss (TEWL) is a measurement of the water loss from a body that passes through the skin epidermis through diffusion, which then evaporates into the atmosphere. This measurement is used to define skin barrier characteristics. Reduction of TEWL (lower TEWL readings) indicates that the skin barrier is more effective in retaining moisture in the skin, possibly enabling it to feel more moisturized. Ideally, products that exhibit and maintain skin TEWL reduction over time are most desirable. If the TEWL is high, this means that the skin barrier is less effective in retaining moisture.

A study [3] conducted by International Research Services, Inc. (Port Chester, NY), on 21 subjects, measured TEWL at baseline, 1, 2 and 4 hours after a single product application (2.0 mg/cm^2) to the lower leg. Each panelist received treatment of a skin lotion with 2% LaraCare® A200 on one leg and placebo (same formulation without LaraCare® A200) on the other leg. TEWL was measured with the DermaLab Meter (Cortex Technology, Denmark). Data is given in Figure 3.

Although each formulation reduced the TEWL after 1 hour, only the test product containing 2% GA maintained a statistically significant reduction (Student's t-test, 95% CL) from baseline at 2 and 4 hours. It appears that GA may have imparted some additional film-forming properties to the applied formulation which then helped to maintain skin barrier properties.

Figure 3. Reduction of TEWL



Fine Lines and Wrinkles

International Resources, Inc. conducted a study [4], using 15 panelists, to evaluate the effect of GA upon fine lines and wrinkles in the crow's feet area of the face. Contour analysis provides a method for quantifying skin augmentation, an example of which is the cosmetic action of moisturizer to reduce superficial fine lines. Skin replicas of the test area are prepared using a silicone-based resin that cures and stays intact after application and removal. These casts of the replicas are analyzed. Only one side of the face was analyzed.

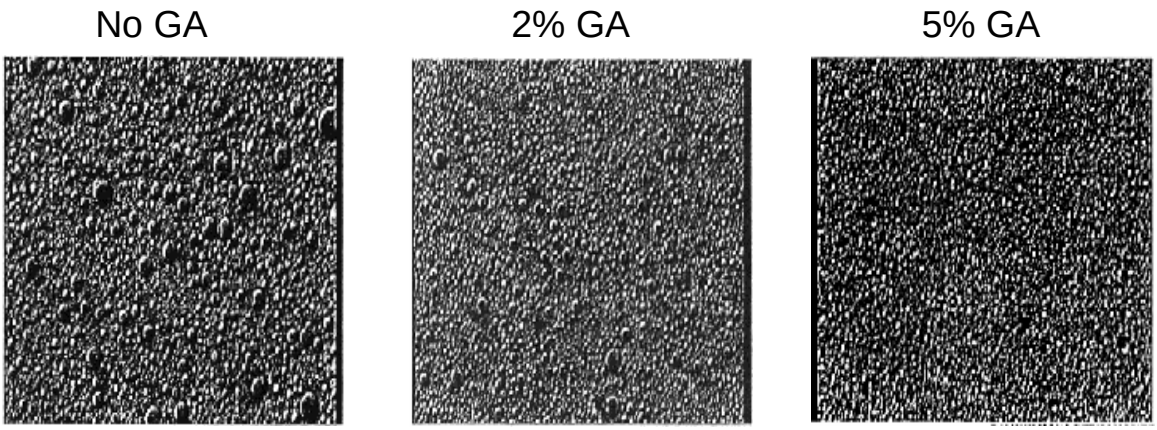
For this study, the skin replicas were analyzed at baseline, prior to any product treatment. New skin replicas of this area were prepared to test the effect of eight weeks of daily, self-administered product treatment. Results of the replica analysis showed a 19% reduction of the appearance of fine lines and wrinkles. This may possibly be attributed to GA's film-forming properties. Here, it may work by filling in or covering some of the superficial fine lines.

Also, research by Trommer and Neubert shows the potential of some polysaccharides to provide anti-oxidative properties to help protect skin against uv-induced oxidative damage [5]. This is interesting since oxidative damage by free radical attack decreases cell function and can lead to skin aging. Since this study shows the topical effect of acacia gum (a mixture of galactoarabinan oligosaccharides, polysaccharides and glycoproteins), to decrease the formation of secondary lipid peroxidation products, it may be possible that the GA portion of the acacia gum contributes to some of the skin protection activity seen here.

Emulsion Stability Enhancement

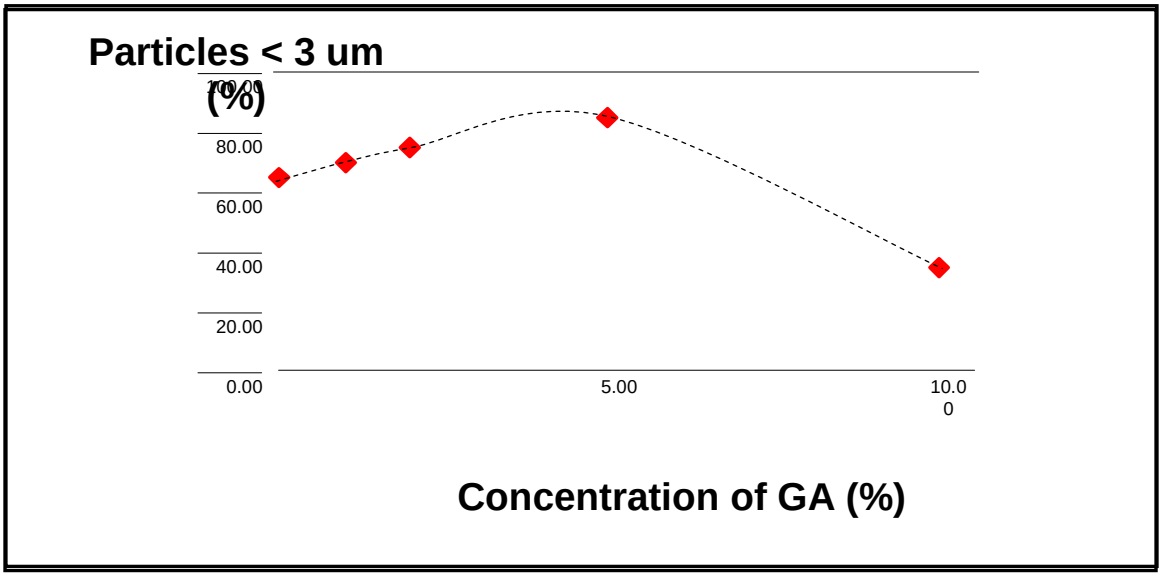
Stokes' Law teaches that having a smaller oil droplet size present in the formulation increases the likelihood for emulsion stability. Larger oil droplets tend to migrate up towards the product surface. Smaller droplets reduce the tendency for the emulsion creaming and separating. A typical oil-in-water emulsion was prepared using different levels of GA. The results given in Figure 4 show that incorporation of 5% GA enabled oil droplet reduction to approximately 2-3µ. Although different emulsifiers are expected to give different results, Laser Diffraction Micro-Spectrometer shows the impact of galactoarabinan on the frequency of the emulsion droplet size in Figure 5. GA may be working with the primary emulsifiers in the formulation to stabilize emulsions. It is known that a greater number of smaller droplets definitely improve emulsion stability [6]. A narrower, small particle size distribution reduces the likelihood of droplet flocculation which can eventually lead to total breaking of the emulsion [6].

Figure 4: The Effect of Galactoarabinan upon Oil Droplets



400X, Nomarski Prism Analysis with Horiba LA 500

Figure 5: The Frequency of Smaller Oil Droplets as a Function of Galactoarabinan



Dispersibility of Crystalline UV Filters

The improved dispersibility of inorganic sunscreen particles in the formulation may possibly enable a more uniform and effective sunscreen layer transferred down onto the skin surface. This improved dispersibility implies less 'clumping' of the particulates. In this case, there may be more efficient packing of the particles for more effective sun protection per specified level of uv filter.

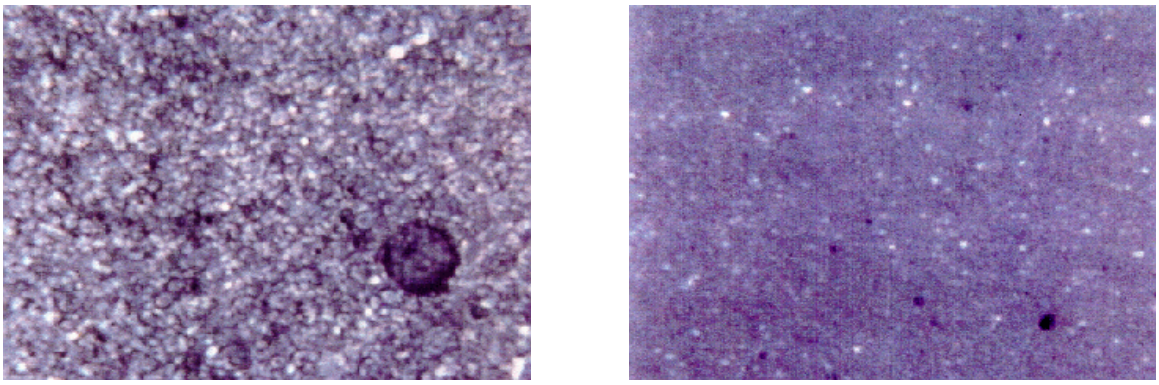
Galactoarabinan appears to facilitate titanium dioxide dispersibility in a lotion formulation. See Figure 6. Some laboratory data shows that GA is able to reduce interfacial tension [7]. Surface tension reducing properties are not comparable with synthetic surfactants but are very similar to natural gums of similar character. Also, due to its molecular shape (a bulky polysaccharide), GA may help reduce the tendency for TiO2 inter-particulate interaction, by imparting some steric hindrance [7]. Some adsorbed neutral polymers may prevent particle attraction [8]. Both of these aspects may help

prevent attractive forces between the inorganic particles and reduce the likelihood of aggregation. So, the primary particles remain. Therefore, a uniform dispersion can be made with little agitation, i.e., no high shear is required.

Incorporation of GA into sunscreen compositions has also been shown to enable an SPF enhancement to these formulations [2]. This research shows that this attribute may be explained by the combination of the improved particulate dispersibility, smaller emulsion or organic sunscreen droplet size and film-forming properties of GA.

Figure 6: The Effect of Galactoarabinan upon Titanium Dioxide Dispersion in a Lotion Formulation

3% $Ti0_2$ | 3% $Ti0_2$ with GA



Formulation Guidelines

LaraCare® A200 is easily dispersible in the water phase of the formulation. Most GA dispersions, up to 5%, will appear cloudy. It is best to add it to the water alone, prior to adding any of the other ingredients. For example, LaraCare® A200 is not soluble in propylene glycol. It also must be dispersed in the water phase, prior to creation of the emulsion, in order to see an enhancement in oil droplet size reduction or formation of a narrower size distribution. GA is expected be stable during exposure to typical emulsion processing conditions, e.g., 75 ºC for 30 to 45 minutes. Formulations including GA have not been seen to be affected by high shear. LaraCare® A200 is also stable in formulations at pH 3 – 13 and can tolerate up to 16% NaCl.

Typically, LaraCare® A200 itself is not expected to affect formulation viscosity. However, according to some feedback from applications work [9], GA may affect product viscosity when incorporated in combination with certain ingredients in personal care formulations. GA may actually impart some viscosity control (some viscosity decrease) when in the presence of various carbomers, polymeric emulsifiers or sclerotium gum. Conversely, LaraCare® A200 has also been reported to increase viscosity of some inorganic sunscreen-type (with titanium dioxide) formulations that already include combinations of xanthan gums and magnesium aluminum silicates.

Typical Starting Formulations

Some typical starting formulations that contain LaraCare® A200 are given in Tables 1-2.

Table 1: Sample Moisturizer Formulation

INCI / Chemical Name	Amount (%)
Phase A	
DI water	79.80
Propylene glycol	2.50
Galactoarabinan (LaraCare® A200)	2.00
Phase B	
Stearic acid	2.00
Isopropyl myristrate	7.50
Cyclomethicone	3.00
Cetearyl alcohol and ceteareth-20	2.00
Phase C	
Triethanolamine	0.60
Phase D	
Geogard 361	0.60
1. Add LaraCare® A200 to water. Start heating to 75 ºC. When LaraCare® A200 particulates have dissolved, complete Phase A. Keep at 75 ºC. 2. Prepare Phase B at 75 ºC. 3. Add Phase B to Phase A with homogenization. Mix for ~ 10 min. 4. Cool to 40 ºC. 5. Add Phases C and D.	pH=7.42 Viscosity = 6,400 cps (Brookfield HAT Viscometer 10 rpms/ 3 rotations with upwards motor)

Table 2: Sample Sunscreen Formulation

INCI / Chemical Name	Amount (%)
Phase A	
DI water	62.48
Galactoarabinan (LaraCare® A200)	2.00
Propylene Glycol	2.50
Polyacrylamide and C13-14 Isoparaffin and Laureth-7	3.00
Phase B	
Glyceryl stearate and PEG-100 stearate	2.00
Glyceryl dilaurate	2.00
Isopropyl myristrate	7.50
Cetearyl alcohol and ceteareth-20	2.00
Dimethicone	1.00
Methylsiloxane fluid	3.00

Benzophenone-3	4.00
Octyl methoxycinnamate	7.50
Phase C	
Geogard 361	0.60
Phase D	
10% Sodium Hydroxide (pH adjust)	0.42
1. Add LaraCare® A200 to water. Start heating to 75 ºC. When LaraCare® A200 particulates have dissolved, complete Phase A. Add Polyacrylamide and C13-14 Isoparaffin and Laureth-7 last in Phase A. Keep at 75 ºC. 2. Prepare Phase B at 75 ºC. 3. Add Phase B to Phase A with good mixing. Mix for ~ 15 min at 75 ºC. 4. Cool to 40 ºC. 5. Add Phase C 6. pH adjust to 6-7	pH=6.43 Viscosity = 20,480 cps (Brookfield HAT Viscometer 10 rpms/ 3 rotations with upwards motor)

Toxicology and Regulatory

A human repeat insult patch test [10] (RIPT) was conducted by International Research Services, Inc. (Port Chester, NY) on 58 individuals to assess irritation potential on skin from use of LaraCare® A200. Test material (0.025 mls of 10% solution) on the 8 mm^2 patch was applied three times per week for a total of 10 applications on the backs of the subjects. There was no statistical evidence of irritation or sensitization from this material.

The Neutral Red Uptake Bioassay was used to assess the toxicity of LaraCare® A200 to normal human epidermal keratinocytes (NHEK). The reduction in neutral red uptake of 50% (NRU_{50}) was determined to be 3,650 µg/ml. Relative to the positive control, sodium lauryl sulfate (NRU_{50}= 4.18 µg/ml), LaraCare® A200 appears to be very mild to human epidermal keratinocytes.

LaraCare® A200 has also been approved for use in major areas of the world.

Conclusion

Galactoarabinan, a naturally-occurring polysaccharide, provides many desirable skin care effects (TEWL reduction and reduction of the appearance of fine lines and wrinkles). In addition, it contributes to improved formulation aspects such as a smaller, emulsified oil droplet size and a uniform dispersion of inorganic sunscreen agents.

References

[1] Galactoarbinan “Folklore Chapter”-publication anticipated in future—and correspondence from Bryan Rodriguez, Lonza, Inc., 2006.

[2] Kasprzyk, E., and Siegler, L., Galactoarabinan as a Natural SPF Booster, *Cosmetics and Toiletries* 121 10, 55-61 (2006).

[3] Data on file.

[4] Data on file.

[5] Trommer, H. and Neubert, R., The examination of polysaccharides as potential antioxidative compounds for topical administration using a lipid model system, *International Journal of Pharmaceutics*, 298 153-163 (2005).

[6] Becher, P., “Emulsions Theory and Practice”, 2nd Ed., (Kreiger, 1977) p. 49, 170.

[7] Laboratory Data from M. Serpil Kislalioglu, Cosmetics and Toiletries Technology Graduate Program, College of Pharmacy, University of Rhode Island, Kingston RI June – December, 1995.

[8] Hem, S., and Weiner, N., Course Notes from *Emulsion Suspension Technology*, March 2000. p. D-4, G-16.

[9] Correpondance from Elzbieta Kaprzyk, Tri-K Industries, Dec. 2006, Feb 2007.

[10] Data on file.