

Cariflex™ Isoprene Rubber (IR) for Medical Stoppers

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Kraton Performance Polymers, Inc. contracted a 3rd party laboratory to conduct a medical stopper study to compare the performance of halo-butyl rubber against two major synthetic polyisoprene types: Ziegler-Natta IR, and Cariflex IR, which is produced through an anionic process. Polyisoprene elastomers, such as Cariflex IR, are synthetic, predominantly stereo regular, and resemble natural rubber in molecular structure and properties. The study showed that medical stoppers made with Cariflex IR could easily pass the extraction test under Japanese Pharmacopeia (JP) 7-03 (XV revision 2006), herein referred to as JP, which is the most stringent protocol, while Ziegler-Natta IR failed or only marginally passed. To inquire about the complete study, please contact cariflex@kraton.com.

Abstract

There are two major synthetic polyisoprene types with high cis-1, 4 content. They include Ziegler-Natta IR, polymerized in the presence of a titanium/aluminum catalyst, and anionic IR, which is polymerized with an alkyl-lithium initiator. These different processes yield different products.

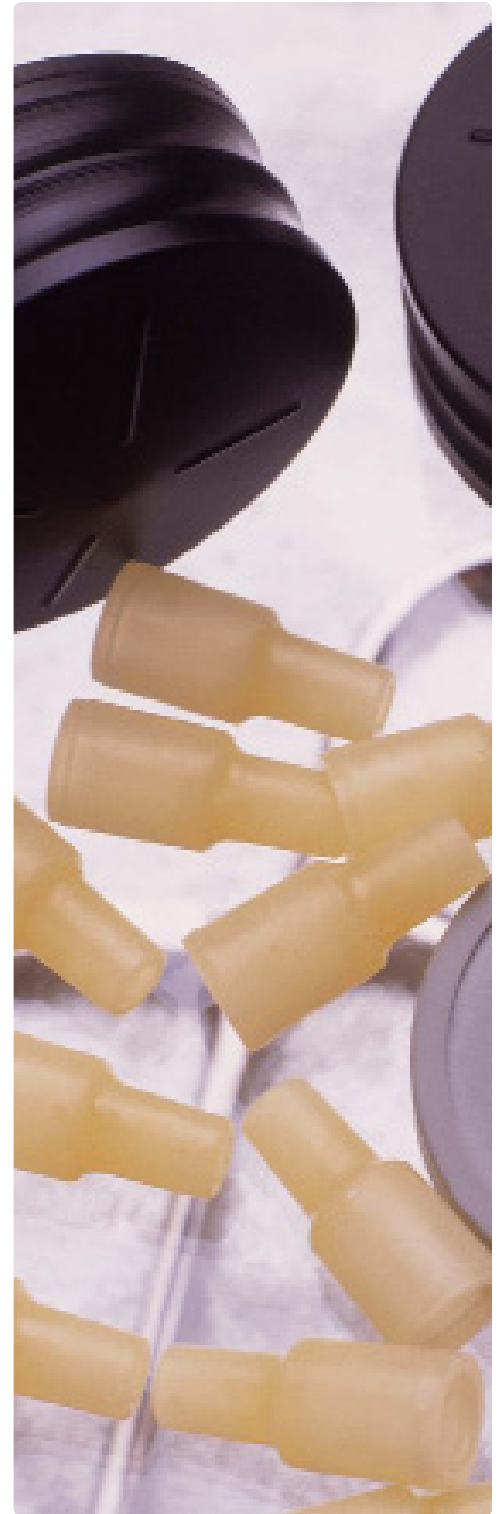
Cariflex IR offers many features and benefits including protein-free, low residual metals, low gel content (~0 %), odor-free, and excellent coring properties (low risk of fragmentation). Cariflex IR is a highly clean rubber, which therefore can be used in medical stopper closures for glass and plastic infusion bottles, IV bags, and vials (where high gas barrier property is not essential).

Cariflex Polyisoprene Products

Multiple formulations based on Cariflex IR0307, Cariflex IR0310, Ziegler-Natta IR, and halo-butyl rubber were used to produce stoppers of equivalent hardness. The extraction testing protocol included JP, which can also be related to the Chinese medical standard (YBB 00042005). Test results were determined in a two-part extraction series. In the Series 1 test, Cariflex IR0307 and IR0310 gave lower KMnO₄ reducing substances than Ziegler-Natta IRs and easily passed JP. Ziegler-Natta IR (ZN-IR-A, general purpose grade) failed the JP extraction test. Ziegler-Natta IR-B, medical grade, was marginal to pass the JP extraction test (limited safety margin). In Series 2, Cariflex IR0307 gave consistent results in the extraction test and passed all JP specs. Ziegler-Natta IR-C medical grade failed to meet JP specs. Bromo-butyl rubber (BR-IIR-B) gave low level of extracts and passed JP specs, but slowly released impurities during ageing and was inferior in gamma radiation resistance.

Summary and Conclusion

Cariflex IR based medical stoppers can easily pass the extraction test under JP, which is the most stringent testing protocol. Ziegler-Natta IR medical grades did not always meet JP specs. Halogenated butyl rubbers gave much lower oxygen and moisture permeability than IR rubbers. However, they generated more extractables as the polymer degraded in long-term service life. Halogenated butyl rubbers were readily degraded by gamma ray radiation, while IR rubbers were much more stable. Cariflex IR based medical stoppers allowed even lower needle insertion force than Ziegler-Natta IR based stoppers. This could have been related to the lower elastic modulus of Cariflex IR than Ziegler-Natta IR. Cariflex IR based medical stoppers gave outstanding performance in the coring test, better than any other rubber stoppers, which eliminated concerns about contamination of rubber fragments into liquid drugs. Cariflex IR can be used for IV bags and vial stoppers where high gas barrier property is not necessary.



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