

AST-120 (Spherical Carbon Adsorbent): A Novel, Engineered Carbon Microsphere Product for Use in Chronic Inflammatory Bowel Disease and Liver Dysfunction

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Background:

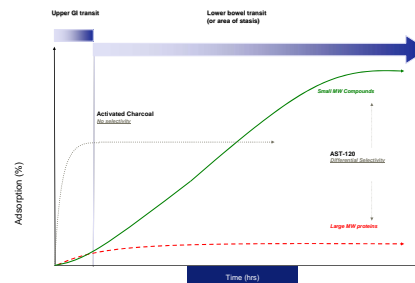
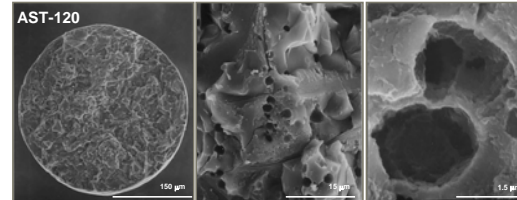
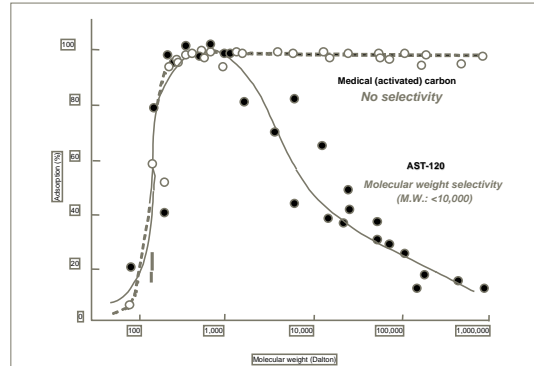
- AST-120 is currently in clinical trials for fistulizing Crohn's disease, Pouchitis, IBS, PPI-Resistant GERD, and Hepatic Encephalopathy.
- AST-120 consists of microspheres 200-400 μm in diameter with an extremely high specific surface area of > 1600 m^2/g .
- The microspheres consist of a carbon scaffold (> 94% carbon) with a defined acidic/alkaline functionality at the surface, which has been optimized to adsorb select low MW pro-inflammatory mediators.
- The bulk of the adsorptive surface resides in the interior of the microspheres, providing a highly porous network of channels.
- The kinetic profile of AST-120 is optimized for binding in the lower GI tract.
- The low MW specificity and lack of binding to GI proteins (e.g. digestive enzymes) make AST-120 suitable for chronic use.

Methods:

- 10mg/dL solutions of test compounds were prepared in pH 7.4 phosphate buffer.
- AST-120 or activated charcoal (AC, USP) were suspended in above buffer systems at 50 mg/mL for low MW organics and at 2.5 mg/mL for higher MW proteins.
- Suspensions were incubated for 3hr under constant agitation at 37°C (lipase, chymotrypsin and trypsin experiments conducted at 21°C).
- Residual analyte was detected by total organic carbon or UV₂₈₂ spectrometry and quantitated against appropriate controls.

Discussion:

AST-120 is a new physical entity and has been designed to specifically adsorb low molecular weight inflammatory mediators and GI stimulants. In contrast to activated charcoal, AST-120 can be used on a chronic basis and delivers the bulk of adsorptive capacity to the lower GI tract. AST-120 represents a first in class oral adsorbent which has an inherent sustained binding profile. AST-120 has significantly reduced binding affinity to higher MW proteins, especially digestive enzymes, allowing patients to maintain nutritional status while on chronic courses of therapy.



AST-120 Binding Profile

Compound Class	Affinity
Bile Acids / Fatty Acids	High
Indoles / Phenols (TRP, IS, Histamine, 5-HT, Tryptamine, Tyramine, Caffeine, Octopamine)	High
Free Radical Generators (NaMBS, FMLP, NO)	Medium-High
Other Low MW Organics / ions (NH_4^+ , AIBA, AG, DMA, Putrescine, Creatinine, 33mer gluten hapten)	Medium-High

AST-120 vs. Activated Charcoal

Compound	AST-120	Activated Charcoal, USP
DL- β -aminoisobutyric acid	88.0	41.9
Aspartylglycine	93.3	82.7
Dimethylamine	49.8	22.0
Putrescine	83.9	72.4
Guanidinosuccinic acid	64.1	66.6
Creatinine	96.0	95.9
Indoleacetic acid	97.3	97.5
p-hydroxyphenylacetic acid	96.6	98.4
α - amylase	2.7	99.9
Pepsin	7.1	99.7
Lipase	30.6	99.4
Chymotrypsin	10.2	99.6
Trypsin	4.3	99.5