

## AST-120: 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  $\mu\text{m}$  in diameter with an extremely high specific surface area of  $> 1600 \text{ m}^2/\text{g}$ . 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 product, providing a highly porous network of channels inside the microspheres. The engineered design of AST-120 has created a broad-spectrum oral adsorbent (compounds  $< 10\text{kD}$  MW) which can be administered on a chronic basis. This study details differential features of AST-120 that support clinical applications 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 UV<sub>282</sub> spectrometry and quantitated against appropriate controls. Results: Normalized % removal from solution in a head-to-head comparison of known inflammatory mediators and digestive enzymes (bold) are presented in the table below. Discussion: The binding kinetics of AST-120 are delayed, thus allowing use of concomitantly administered medications without altering PK or absorption profiles. AST-120 represents a product that binds putative pro-inflammatory mediators to an equivalent or greater extent than Activated Charcoal, with significantly reduced binding affinity to higher MW proteins, especially digestive enzymes, allowing patients to maintain nutritional status during chronic courses of therapy.

Compound	AST-120	Activated Charcoal, USP
DL- $\beta$ -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
$\alpha$ - 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