# Glatiramer Acetate (GA) Produced by Mapi Pharma is Equivalent to Commercially Available GA Preparations

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## BACKGROUND

Glatiramer Acetate (GA) is one of the first disease modifying treatments approved for relapsing-remitting multiple sclerosis. Recently, several generic equivalents of GA were approved for marketing in the USA. Mapi is developing GA to be used in Glatiramer Acetate Depot (GA Depot) and in Mapi's generic GA. Here, we present key characteristic data from physicochemical (structural) and biological (pharmacodynamic) assays that were conducted to compare Mapi's GA and all US-approved GA equivalents.

## OBJECTIVE

To demonstrate through the results (physicochemical and biological) that Mapi's GA is similar to US-approved and commercially available GA equivalents.

## DESIGN/METHODS

Mapi's GA is produced using the same starting materials and basic chemistry as Copaxone®. At least five batches of Copaxone®, one batch of Glatopa™ (Sandoz), one batch of Glatiramer Acetate Injection (Mylan) and several batches of Mapi's GA were analyzed for physicochemical properties (molecular weight distribution, impurities profile, amino-acid composition and spectral fingerprint) and various structural signatures. A representative batch of Mapi's GA was compared with three different commercially available GA preparations using a bioassay test (MOG-induced EAE in mice).

## RESULTS

The selected tests and data presented here represent a portion of a broader set of physicochemical and biological assays that were conducted. No differences were observed in the physicochemical properties or the structural signatures between Mapi's GA and all other US-approved GA equivalents (Figures 1, 2). Equivalent pharmacodynamic activity of Mapi's GA to commercially available GA preparations (Copaxone®, Glatopa™ and Glatiramer Acetate Injection) was demonstrated using MOG-induced EAE in mice (Figure 3, table 1).

**Figure 1: Chromatograms of molar mass distribution test for Mapi GA and Copaxone®**

Figure 1 shows the overlay of the molar mass distribution test result for lots of Mapi GA and Copaxone®, demonstrating the equivalence of this attribute in both materials

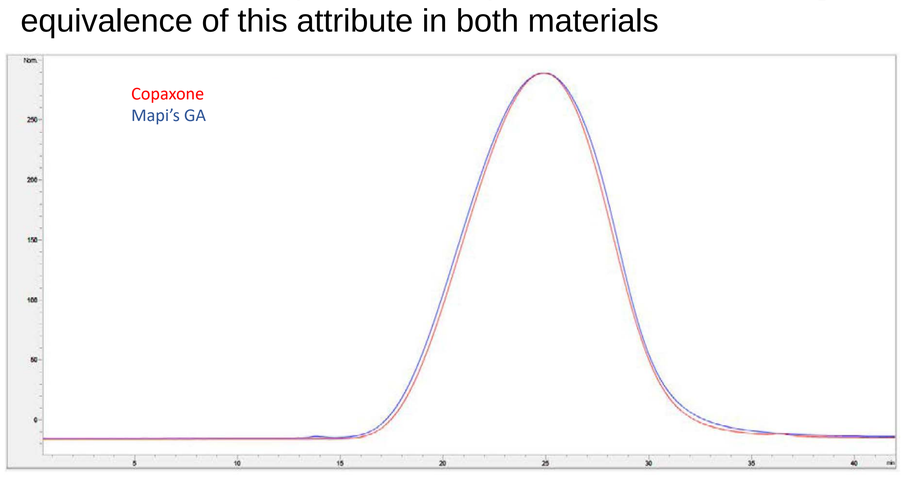



***Figure 2:* Amino acid analysis results of GA samples**

GA samples were analyzed according to USP <1052> 2% (20mg/mL) solutions were used for this test: commercial Copaxone®/Glatopa™ lots and Mapi GA 20mg/mL solution in water. All samples presented similar molar fractions for the 4 amino acids within the precision of the analytical method (precision of each result is ±5%)

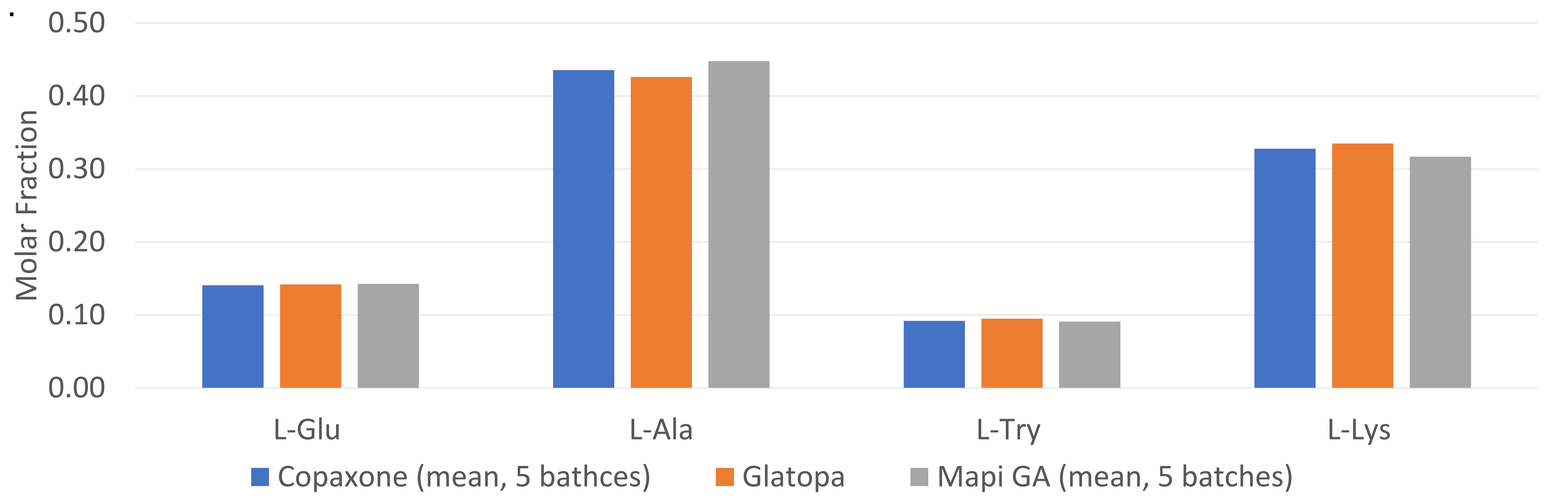
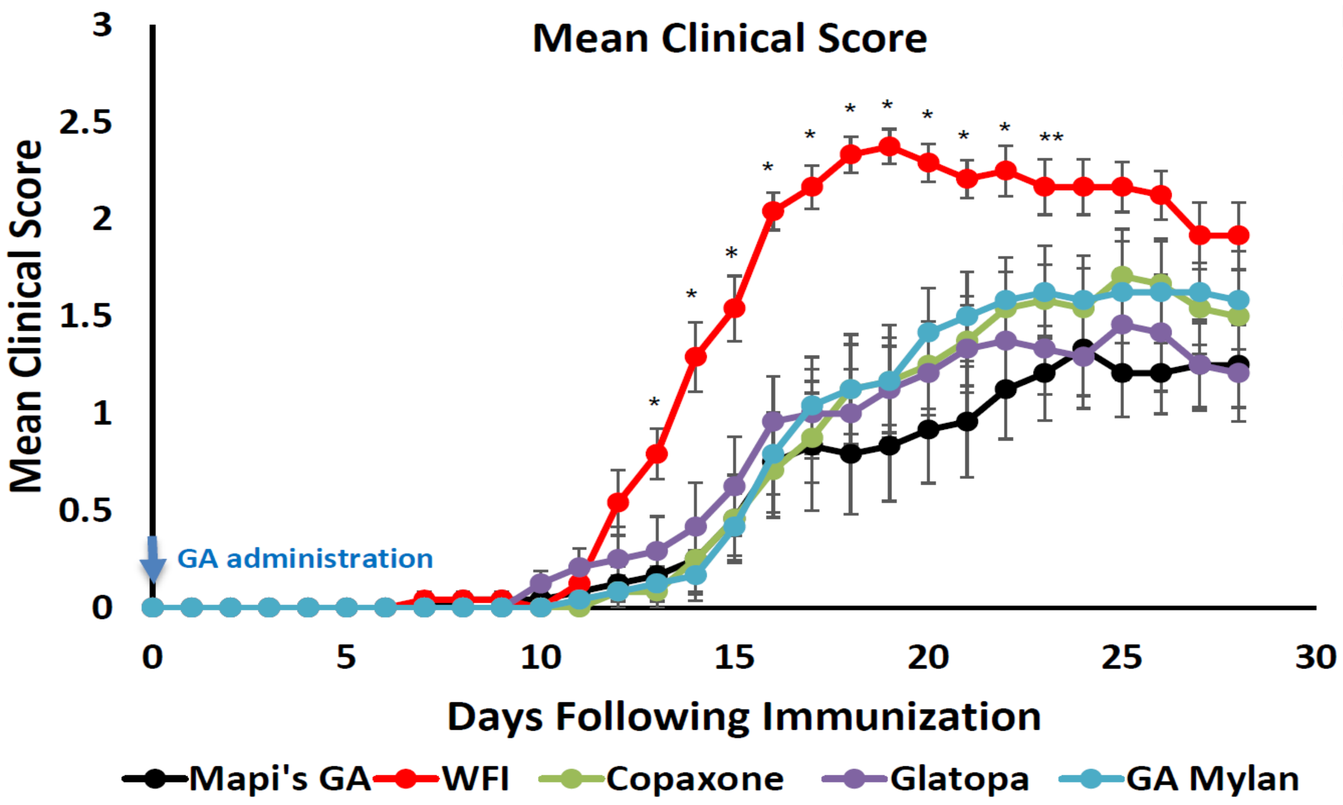



***Figure 3: Effect of Mapi GA on MOG-induced EAE compared to commercially available GA preparations***




**P<0.05 for all groups compared with WFI (untreated control) group. ** P<0.05 for all groups Except GA Mylan compared with WFI (untreated control) group. Single Factor ANOVA followed by two-tailed T Test assuming equal variance. n=12 / group, +/- standard error.*

MOG-induced EAE was used to demonstrate the equivalence of the biological effect of Mapi's Glatiramer Acetate (GA) to that of commercially available GA injections (Copaxone®, Glatopa™ and Glatiramer Acetate Injection). All test articles were injected SC at a dose of 0.5 mg together with the disease induction emulsion. All test articles exerted the same attenuation effect on EAE symptoms, in a statistically significant manner compared with untreated control (figure 3 and table 1). It is concluded that Mapi's GA has an equivalent biological effect as commercially available GA preparations.

***Table 1: Effect of Mapi GA on MOG- induced EAE compared to commercially available GA preparations- calculated values***

| Groups | Maximum Mean Disease Score | Mean Disease Duration | Mean Day of Onset | AUC Clinical Score | Survival Rate at Day 28 |
|---|---|---|---|---|---|
| WFI | 2.45±0.08* | 16.67±0.43* | 12.33±0.43* | 31.58±1.45* | 100% |
| GA Mapi | 1.5±0.23 | 10.16±1.78 | 18.83±1.78 | 14.25±3.34 | 100% |
| Copaxone® | 2.00±0.17 | 11.50±1.29 | 17.50±1.29 | 17.71±2.49 | 100% |
| Glatopa ™ | 1.59±0.31 | 12.17±1.68 | 16.83±1.68 | 17.27±3.14 | 100% |
| GA Mylan | 1.82±0.27 | 11.92±1.35 | 17.08±1.35 | 18.33±2.84 | 100% |

**P<0.05 compared with all other groups, Single Factor ANOVA followed by two-tailed T Test assuming equal variance. n=12 / group, +/- standard error.*

## CONCLUSIONS

Mapi's GA is equivalent to commercially available GA products in physicochemical properties, structural signatures and biological activity as demonstrated by bioassay and complies with the FDA's guidance for generic GA. These results will support GA Depot and a new generic GA version commercialization by Mapi Pharma.

## DISCLOSURES

Nadav Bleich Kimelman, Shai Rubnov (co-inventor of GA Depot), Susanna Tchilibon, Laura Popper and Uri Danon are employed by Mapi Pharma. Ehud Marom is a co-inventor of GA Depot, and founder and CEO of Mapi Pharma.