

## Summary of Endorphinate® Induced Clinical Pain Trial Results

### Cold Pressor Protocol

The cold pressor induced pain methodology is a generally accepted standard for testing opioid-level<sup>1</sup> pain relief. (c.f. [FDA Approved Cold Pressor Clinical Trials](#)). A Jeitech RW-3025G Refrigerating Bath maintained water at constant temperature. Subjects were asked to keep their non-dominant hand fully submerged in 2° C water for as long as possible. Pain tolerance was measured by the duration of time the subject kept their hand submerged, with a limit set at 4 minutes.

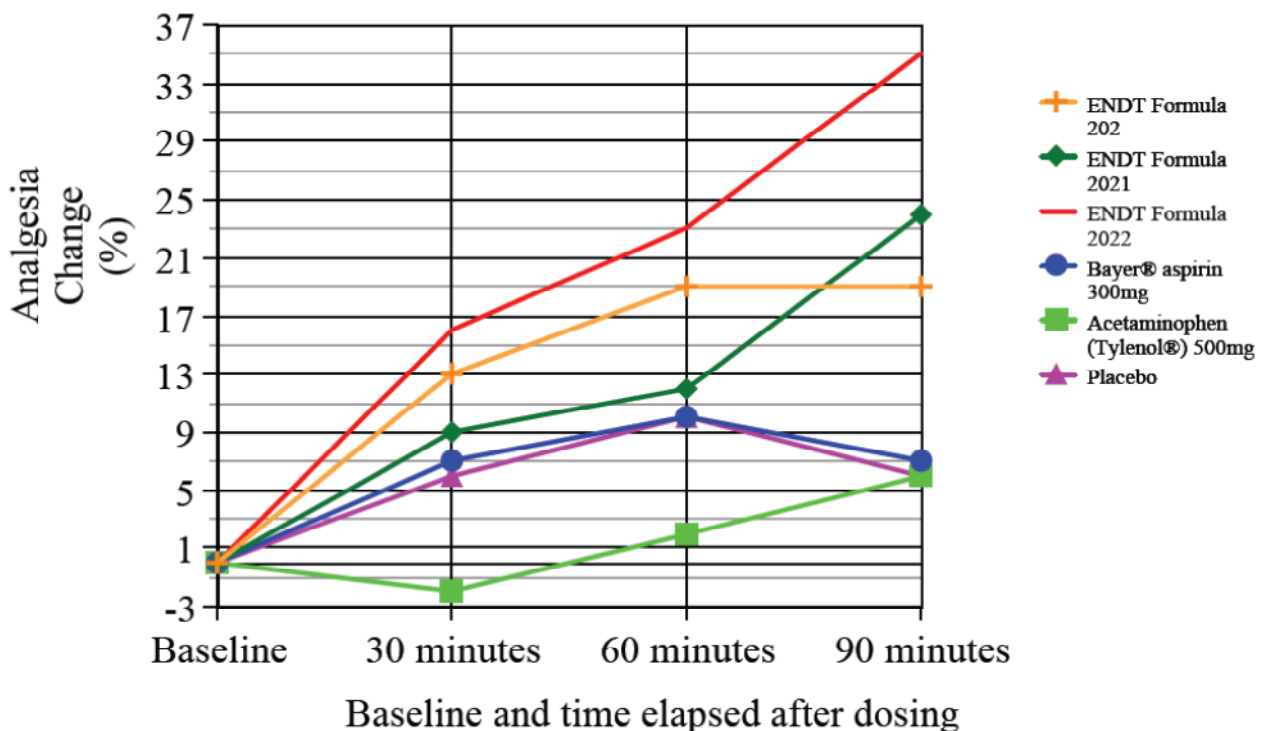
### Results

#### Endorphinate® Formulations

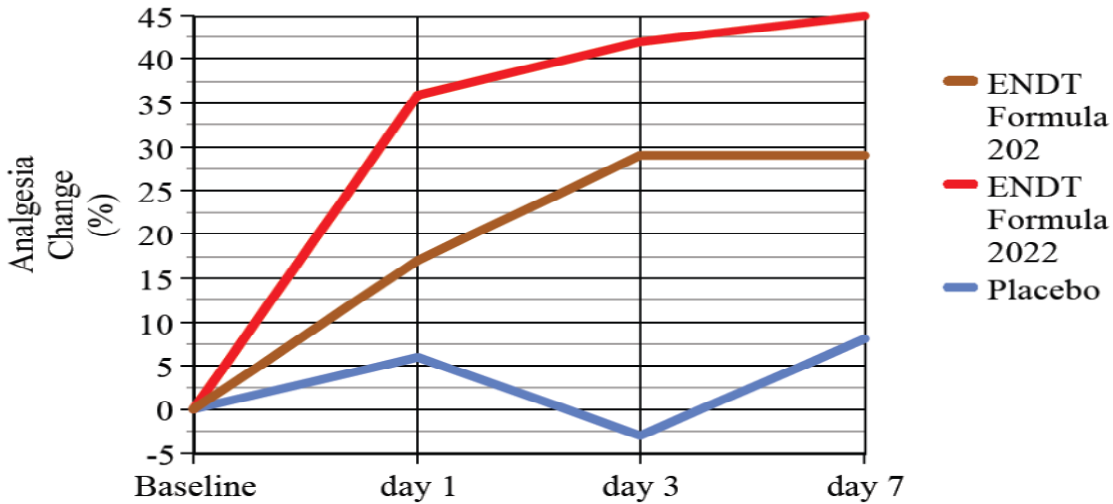
ENDT 202: NAC + Ginkgo Biloba	ENDT 2021	NAC + Ginkgo Biloba + DLPA
ENDT 203: NAC + Glutamic Acid	ENDT 2022	NAC + Ginkgo Biloba + WWB <sup>2</sup>
ENDT 302: MSM + Ginkgo Biloba	ENDT 212:	NAC + Guarana + Ginkgo Biloba
ENDT 303: MSM + Glutamic Acid	ENDT 2122:	NAC + Guarana + Ginkgo Biloba + WWB

#### Graphic Summaries

Graph 1. Cold pressor induced pain study comparing Endorphinate® (formulae 202, 2021 and 2022) with Tylenol®, Bayer® aspirin and placebo. Temperature maintained at 2°C by Jeitech RW-2025G refrigerating bath. (12 subjects)

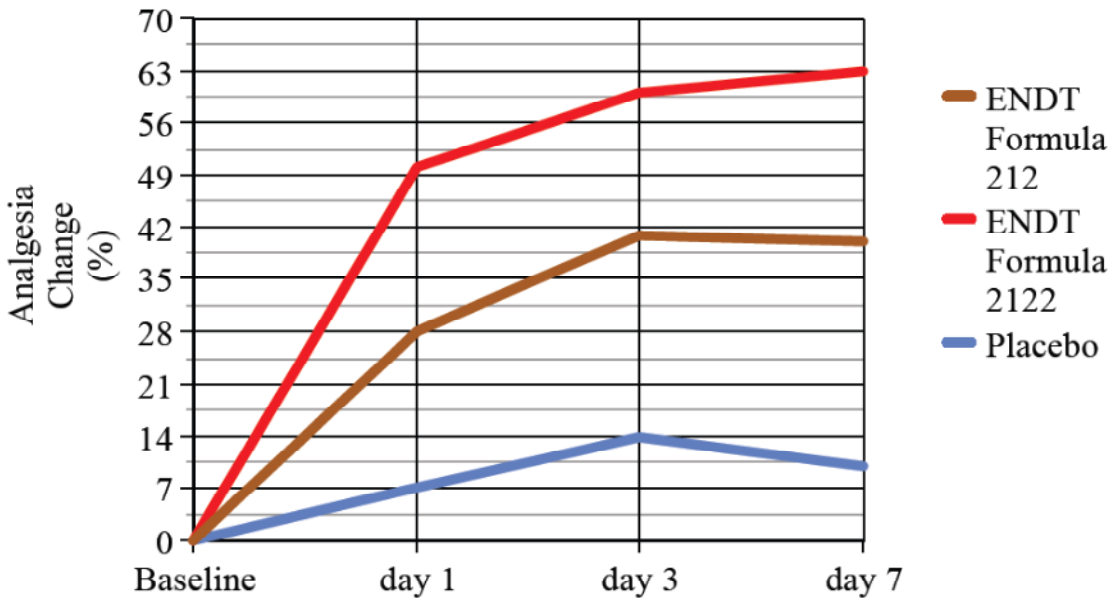


Graph 2. 7-day cold pressor induced pain study comparing Endorphinate® (formulae 202 and 2022) with placebo. Temperature maintained at 2°C by Jeiotech RW-2025G refrigerating bath. (8 subjects)



Baseline recorded before dosing; other measurements recorded 1 hour after 2d dosing of specified day.

Graph 3. 7-day cold pressor induced pain study comparing Endorphinate® (formulae 212 and 2122) with placebo. Temperature maintained at 2°C by Jeiotech RW-2025G refrigerating bath. (8 subjects)



Baseline recorded before dosing; other measurements recorded 1 hour after 2d dosing of specified day.

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<sup>1</sup> It is interesting to compare these results to cold pressor studies of Vicodin<sup>®</sup> and oxycodone. (*Randomized Double-blind Placebo Controlled Crossover Study of Acetaminophen, Ibuprofen, Acetaminophen/Hydrocodone, and Placebo for the Relief of Pain From a Standard Painful Stimulus*, Academic Emergency Medicine, Volume 16, Issue 9, pages 911–914, September 2009 ([Vicodin<sup>®</sup>/OTC Cold Pressor Induced Pain Study](#))). *The hypoalgesic effect of oxycodone in human experimental pain models in relation to the CYP2D6 oxidation polymorphism*, Basic Clinical Pharmacology Toxicology (2009), Volume: 104, Issue: 4, Pages: 335-344, [Oxycodone Cold Pressor Induced Pain Study](#). Although the Vicodin<sup>®</sup> study (650mg acetaminophen/10 mg hydrocodone) measured percentage decrease in the amount of pain experienced using the Visual Analog Scale (VAS) rather than pain tolerance (time to hand withdrawal), these measure are typically congruent, as shown in the Oxycodone study. In the Vicodin Study, after 1 hour, Vicodin resulted in a 9.5% decrease in pain experienced, compared to 19% and 23% decrease in pain experienced 1 hour after subjects took ENDT 202 and 2022. The Oxycodone (20 mg) study used both measures, and ENDT compared favorably to the results of that study. Moreover, the Endorphinate formulations showed none of the noxious side effects typically experienced when taking opioid drugs and reported in these (and other) cold pressor studies of exogenous opioids.

<sup>2</sup> White willow bark (WWB) contains salicin, the active ingredient in aspirin. The dramatic synergy demonstrated when WWB is added to the basic ENDT formulation supports the principles, discussed in our [Distress Disorder Pending Patent](#), that the combination of ENDT with over-the-counter pain medications (aspirin, Tylenol<sup>®</sup>, ibuprofen) could provide a highly effective and relatively safe (as compared to opioid narcotics) pain medication.