A Scintigraphy and Pharmacokinetic Study to Evaluate the Absorption and Distribution of Buspirone Hydrochloride from a Triple-Pulse, Timed-Release Tablet.

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ABSTRACT

Objectives: To obtain data for development of a precision-timed release buspirone hydrochloride tablet (CTx-2103) that will provide a once-daily, anxiety treatment. This study elucidated the bioavailability, absorption of buspirone within the GI tract and evaluated the pharmacokinetics of four different release profiles.

Methods: Multi-layered oral tablets formulated utilizing Cingulate's Precision Timed Release® (PTR®) platform and BDD's patented OralogiK™ technology evaluated three timed-release profiles and one IR profile of buspirone. This four-arm, open-label study was conducted in healthy male volunteers. Dosing was separated by a minimum of 7 days.

For the scintigraphy, timed-released doses were radiolabelled with 4 MBq technetium-99m. Abdominal images and blood sampling were evaluated at defined intervals.

Results: Scintigraphic imaging visualised transit of the tablets through the gastrointestinal tract, confirming both the site and onset of release. Mean onset of radiolabel release was 3.87±0.48 hrs., 9.40±1.10 hrs., and 10.1±1.52 hrs for the 4 hr, 8 hr and for the triple-release radiolabelled tablets, respectively. Pharmacokinetic data will be correlated with scintigraphic onset times to establish the full release profile of the tablets.

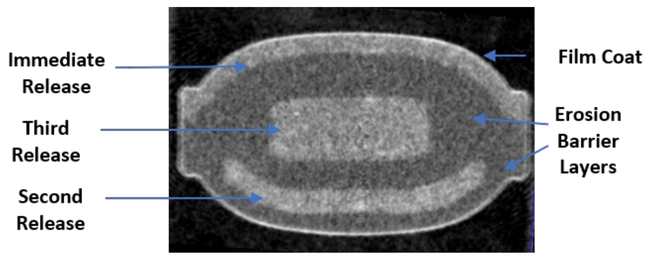
Conclusion: Scintigraphic imaging demonstrated successful timed release of buspirone in the GI tract and pharmacokinetic data will determine bioavailability. Together, this data will inform the precise formulation and release profile of CTx-2103.

Clinical Trial Information: NCT04138498

BACKGROUND

As reported by the National Alliance on Mental Illness (nami.org) anxiety disorders are the most common mental health concern in the U.S. There are a number of therapeutics options for patients' management of anxiety disorders however buspirone is particularly helpful as it is not addictive, does not exert anticonvulsant nor muscle relaxant effects and lacks the sedative effects associated with atypical anxiolytics.

However, with all of its benefits, buspirone in practice is administered two to three times per day. Cingulate® is looking to achieve optimal once-daily dosing using the company's innovative, proprietary, Precision Timed Release (PTR) drug delivery platform technology which incorporates an Erosion Barrier Layer (EBL) providing control of drug release at precise, predefined times. The formulation being tested is comprised of three distinct releases; an immediate release followed by a 4- and 8- hour release profile. The in vitro dissolution characteristics are noted below. This work sets the stage for future formulation of a Precision Time Release platform technology tablet.

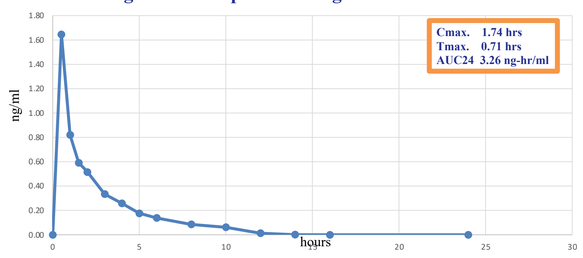


Design of the Cingulate Precision Timed Release® (PTR®) Platform Technology Tablet

Poster Number: 108

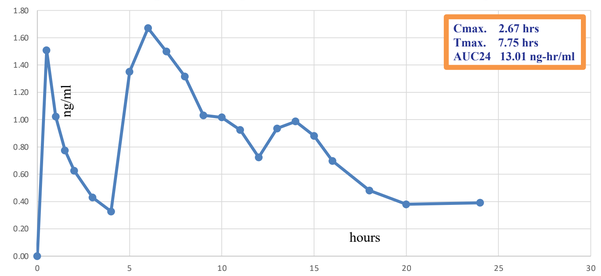
RESULTS

Single Dose Buspirone 10 mg- Immediate Release



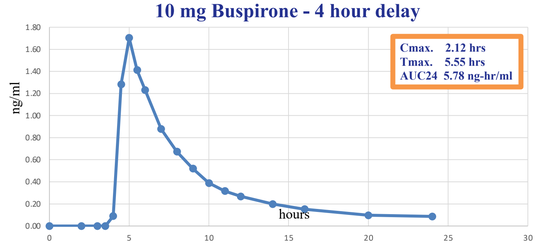
Treatment D: A single tablet releasing 10 mg buspirone HCL (commercially available) immediately

Buspirone Triple Release: Total Dose 30 mg



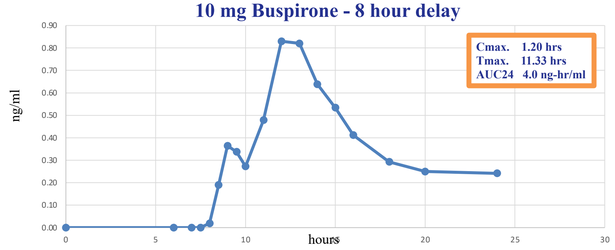
Treatment A: A single triple-release tablet tablet 10 mg of buspirone HCL after at 0, 4, and 8 hours (total dose 30mg buspirone)

10 mg Buspirone - 4 hour delay



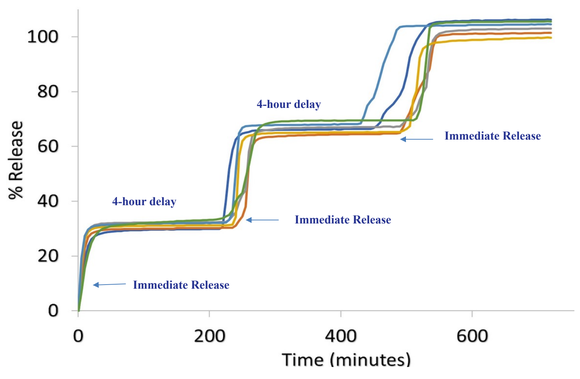
Treatment A: A single timed-release tablet releasing 10 mg buspirone HCL after a 4- hour delay

10 mg Buspirone - 8 hour delay

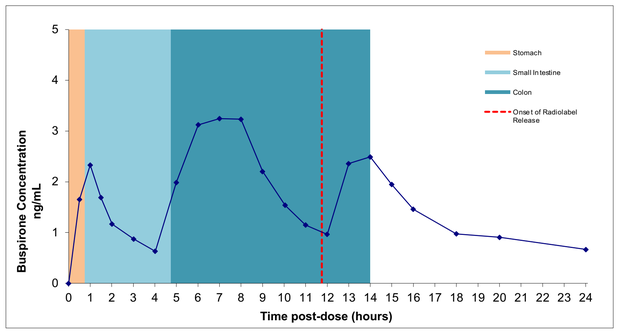


Treatment B: A single timed-release tablet releasing 10 mg buspirone HCL after a 8- hour delay

Tablet Formulation: In Vitro Dissolution Characteristics



Individual Subject: Triple Release Buspirone Formulation



Subject was administered a triple release formulation of buspirone with the intended release profile being 0hrs (immediate), 4hours and 8 hours. The third release was radio-labelled.

SUMMARY AND CONCLUSIONS

1. A once-daily buspirone oral tablet has been designed that delivers three (3) releases of medication at predefined times thus providing the opportunity for entire day efficacy, safety and convenience.
2. Based on the dissolution profile this tablet achieved the solubility required to deliver a triple release of buspirone hydrochloride.
3. This tablet was able to deliver the intended dose at each of the three time points, yielding a total dose 30mg.
4. The tablet accurately delivered the immediate and 4 hour predetermined releases, however the final time point for absorption was approximately 11 hours intended 8 hours).
5. This data demonstrates the ability to deliver a single administration of a triple release buspirone medication setting the stage for future trials employing Cingulate's Precision Timed Release (PTR) Technology.

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