



# Unique Acetium<sup>®</sup> Capsules in Prevention of Migraine Attacks.

Patient Testimonials and a Randomised Clinical  
Trial (RCT)

**BIOHIT HealthCare**

Innovating for Health

## Background

It has been estimated that 15% of the world population is affected by migraines at some point of their life. Prophylactic treatment of migraine patients has twofold goals: i) to reduce the frequency, painfulness, and/or duration of migraines, and ii) to increase the effectiveness of abortive therapy. The efficacy of any currently available preventive therapies is highly variable, however, and in many patients, the attack frequency is not under satisfactory control. Many of these drugs also have untoward side effects that offset their potential benefits.

## Testimonials of migraine patients

Since 2013, testimonials were received by Biohit from migraine patients, reporting that our unique Acetium™ capsule (100mg slow-release L-cysteine) developed for inactivation of acetaldehyde in the achrohydric stomach due to atrophic gastritis and PPIs as well as after alcohol intake ([www.biohithealthcare.com/additional-information](http://www.biohithealthcare.com/additional-information)), proved to be highly effective against migraine attacks (**Table 1**). Their headache attacks disappeared almost immediately after Acetium administration, all of them remaining in complete remission for up to 4-5 years until now.

## Novel study hypothesis

These testimonials prompted us to formulate a novel study hypothesis that could possibly explain these dramatic effects of Acetium™ capsules in migraine prevention. This novel hypothesis is grounding on the fact that, swelling and **dilatation of cerebral blood vessels** is necessary to provoke the attack in this vascular-type of headache. Further, it is known that 1) **Nitric Oxide** (NO) is the final trigger of migraine attack, operating through phosphorylated protein kinase G (PKG) and Ca<sup>2+</sup> channels, slowing the influx of calcium into the cell, which leads to smooth muscle relaxation and **vasodilation**; 2) **histamine** is a potent inducer of NO Synthase, making NO available locally on the vasculature, acting through endothelial H<sub>1</sub>-receptors; 3) histamine is synthesized from histidine in **tissue mast cells**, which are ubiquitous cells and their activation e.g. **in the meninges** has long been suspected to be involved in generating migraine headaches; 4) a potent liberator of histamine from the mast cells is **acetaldehyde**, which, in turn, is effectively **inactivated by** Acetium™ capsules. This led us to rational that i) by eliminating acetaldehyde in the stomach, Acetium™ capsules could ii) block (or reduce below the threshold levels) histamine liberation from the tissue mast cells and ECL (enterochromaffin-like cells) cells in the stomach, thus iii) arresting its multitude of functions, of which vasodilatation is critically involved in the migraine attack.

## Randomized Clinical Trial (RCT)

To validate the novel hypothesis that daily use of Acetium® capsules is an effective means to decrease the frequency of (or completely abort) the headache attacks in migraine patients, we designed a double-blind, randomized placebo-controlled clinical trial comparing Acetium® capsule (slow release 100mg L-cysteine, twice a day) and placebo in prevention of migraine attacks during a 3-month trial period (for details, see the **ANNEX**).

A cohort of 200 voluntary subjects (women and men, with aural or non-aural migraine) were enrolled in the study by 6 neurological clinics in Finland. Before randomization, a 3-month retrospective history and 1-month prospective baseline (run-in) period is used to assess the baseline attack frequency. The treatment period in both study arms is 3 months, followed by a 1-month post-trial observation period. The headache diary is the main research tool used to monitor the efficacy of the test preparations, recording all predefined assessment measures (efficacy, tolerability and safety).

As usual in RCTs, data analyses will be separately for i) Per Protocol (PP), and ii) Modified Intention-to-treat (mITT) groups. Rejection or not of the null hypothesis is based on comparison of the two arms for two primary study endpoints and (to a lesser extent) for a series of secondary endpoints. The **two primary study endpoints** (efficacy measures) are: a) number of migraine attacks (NMA) per evaluation interval (1 month), and ii) number of migraine days (NMD) per evaluation period. Potentially useful **secondary endpoints** include: i) intensity of headache (4-tier nominal scale); ii) attack duration in hours (potentially biased by treatment); iii) drug consumption for symptomatic or acute treatment (NMDs treated with abortive agents and the number of drug administrations for acute therapy); iv) patients' preferences and satisfaction; v) responder rate (proportion of study subjects with >50% improvement in NMA or NMD, as compared to baseline values).

### Potential impact of the new concept

Given that slow release L-cysteine of unique Acetium® capsules (patents and patents pending in several countries) is a natural (semi-essential) amino acid, converted to inert substance (MTCA) in the alimentary tract, it would comprise an ideal means to conduct **migraine prophylaxis for years**, without concern about the **side effects** that are inherent to many of the current treatment modalities. If the efficacy is proved in a formal RCT, the concept of using Acetium® capsules in prophylactic treatment of migraines would represent a **major step forward** in a better clinical control of these frequently intractable syndromes.



**Table 1.** Synopsis of the migraine patients giving spontaneous testimonials on the efficacy of Acetium® capsules in prevention of migraine attacks

Patient	Migraine duration; since	ICD-10 Diagnosis	Attack Frequency	Preventive measures tested before A	Treatment for acute attacks before A	Acetium user since:	Effects on migraine attacks	Attacks returning after Acetium cessation	Current daily Acetium dose that prevents migraine attacks	Need of other medication for migraine
F, 39 y	7 y; 2006	G43.1	2-3/mo	multiple	multiple	2013	disappeared	yes	2 x 1 ; m & e	no need
F, 15 y	6y; 2007	G43.1	2-3/we	no	multiple	2013	disappeared	yes	2 x 1 ; m & e	no need
F, 49 y	14y; 1998	G43.1	3-4/mo	single	single	2012	disappeared	yes	not regularly	decreased

F, female; y, years; ICD, International Disease Classification; G43.1 migraine with aura (classical migraine); mo, month; we, week; A, Acetium® capsules (100mg); m, morning; e, evening



**Annex:**

Study design for RCT:

[www.biohithealthcare.com/Scientific/Study-protocols](http://www.biohithealthcare.com/Scientific/Study-protocols)

Efficacy of Acetium® Capsule in Prevention of Headache Attacks in Migraine Patients. Randomized Intervention Trial with a Medical Device (Acetium® Capsules). (Acetium in Migraine Prevention Study)

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