Marie Skłodowska-Curie Actions
Research and Innovation Staff Exchange (RISE)
Call: H2020-MSCA-RISE-2015

Mastiha treatment for Healthy obese with NAFLD diagnosis
“MAST4HEALTH”

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Nonalcoholic fatty liver disease and steatohepatitis (NAFLD/NASH)

• A spectrum of liver injury beginning from simple steatosis to nonalcoholic steatohepatitis (NASH) that leads to advanced fibrosis and cirrhosis.

• One of the most common liver disorders and a major public health problem in Europe and North America.

• One of the most common complications of obesity and diabetes mellitus in Western populations affecting approximately 50% of diabetics and 76% of obese patients

Raman & Allard, 2006
NAFLD is histologically further categorized into nonalcoholic fatty liver (NAFL) and non alcoholic steatohepatitis (NASH). NAFL is defined as the presence of hepatic steatosis with no evidence of hepatocellular injury in the form of ballooning of the hepatocytes. NASH is defined as the presence of hepatic steatosis and inflammation with hepatocyte injury (ballooning) with or without fibrosis.

Chalasami N et al., Hepatology, 2012; 2005-2023
Pathogenesis

The role of the intestinal microbiota

- The intestinal microbiota may stimulate liver steatosis through
  - the induction of obesity by harvesting energy from otherwise indigestible dietary polysaccharides
  - regulation of gut permeability and stimulation of low-grade inflammation
  - modulation of dietary choline metabolism
  - regulation of bile acid metabolism
  - stimulation of endogenous ethanol production by enteric bacteria.

Arslan, 2014
Risk factors

• Obesity (especially central type),
• Insulin Resistance,
• Type-II diabetes mellitus,
• Dyslipidaemia,
• Hyperuricaemia
• Hypertension
• Total parenteral nutrition
• Rapid weight loss
• Intestinal jejunoileal bypass surgery
Therapeutic approach

• Weight loss through diet and exercise
• Bariatric surgery in obese NAFLD/NASH patients
• No approved specific drugs for the management of NAFLD/NASH
• Only medications to improve the aspects of metabolic syndrome
Natural bioactive phytochemicals as an alternative treatment for NAFLD/NASH

• Some herbal remedies might result in significant improvements in liver enzymes and ultrasound scan values for NAFLD/NASH (Liu et al., 2013).

• Betulinic acid, a pentacyclic triterpene found in many plants, effectively ameliorates intracellular lipid accumulation in liver cells (Quan et al., 2013).
Mastiha as an alternative treatment?

- Mastiha possesses **anti-bacterial activity and potent antioxidant and anti-inflammatory properties.**
- Interestingly it contains **over fifty triterpenes**, mainly **oleanolic** and **ursolic** acids and a plethora of **monoterpenes**.
- Terpenes, nowadays attract the interest of researchers and pharmaceutical companies for clinical studies and applications in the therapy of diseases due to their **antioxidant** potential but also due to their **anti-inflammatory or antimicrobial** properties.
Mastiha as an alternative treatment for NAFLD?

- **Ursolic acid** ameliorates hepatic steatosis, improves lipid metabolism, lowers oxidative stress markers and reduces hepatic inflammatory factors mRNA expression in high-fat diet-induced NAFLD/NASH rats (Li et al., 2014).

- Mastiha contains **quercetin** which has been proven effective in **hepatic steatosis and oxidative stress** (Aguirre et al., 2014), as well as **gallic acid** found to ameliorate impaired glucose and lipid homeostasis in experimental NAFLD/NASH (Chao et al., 2014).
Participants

- Harokopio University (Project Coordinator)
- Queen Mary University of London
- University of Leipzig
- INSERM
- Universita Degli Studi Magna Graecia Di Catanzaro
- University of Novi Sad
- University of East Sarajevo

- FISABIO
- Biotechvana
- Randox
- Intervideo
- Sanofi
- CMGA
- Biocrates
- Perspectum diagnostics
Objectives

• Evaluation of Mastiha as a novel non-pharmacologic treatment for NAFLD/NASH patients
• Provision of powerful tools for the NAFLD/NASH patient management
• Establishment of network activities to support the development of new approaches in NAFLD/NASH treatment and management
• Promotion of international cooperation between research scientists working towards innovation
• Enhancement of the training of the next generation of scientists in state-of-the-art technologies and analytical techniques
## Implementation

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WP1: Management and Recruitment of seconded staff

WP2: A multicenter randomized double blind placebo controlled (parallel arm) clinical trial

WP3: Potential epigenetic alterations in response to Mastiha treatment

WP4: Effects of Mastiha on inflammation

WP5: Blood metabolomic profiles in NAFLD patients

WP6: Genetic markers in response to Mastiha

WP7: Modulation in gut microbiome

WP8: Software development for integration

WP9: Training

WP10: Dissemination and Exploitation of the results