Sativex – The Road to FDA Approval

The Food and Drug Administration (FDA) has approved many treatments for MS to help modify the disease course, treat relapses and manage symptoms, but none are completely effective. Many people living with the disease continue to experience flares, disease progression, and ongoing symptoms. Some turn to alternative medicine to manage their symptoms and increase their quality of life, most often in combination with their prescribed MS treatments. One such treatment is cannabis, or marijuana.

There are many types of chemical compounds in cannabis. Flavonoids are a large family of compounds found in most fruits and vegetables, in large part responsible for their vivid colors. They are important because they have been shown to have beneficial anti-inflammatory and antioxidant effects. Terpenoids (or terpenes) are aromatic chemicals responsible for marijuana’s unique smell. Cannabinoids are the chemical compounds that, when consumed, bind to cannabinoid receptors in the human body and alter nerve transmission in the brain (resulting in marijuana’s psychological effects). The two major cannabinoids in cannabis that have been studied are tetrahydrocannabinol (THC) and cannabidiol (CBD). THC is thought to cause most of the psychological effects of cannabis. CBD has significant medical benefits, but does not make people feel “stoned” and can actually counteract the psychological effects of THC.
**Sativex** (Nabiximols) is a cannabis extract mouth spray that contains equal quantities of THC and CBD. It is used outside the United States for the treatment of MS-related spasticity when a person has shown inadequate response to other treatments or found their side effects intolerable. Sativex can be used in addition to a person's current antispasticity medication. It is administered on the inside of the cheek or under the tongue. The optimum dose varies from person to person, so a titration period is needed when beginning treatment. During this phase, the number of sprays is increased each day until the most effective dose is achieved. This can take a few days or up to two weeks. The most commonly reported side effects are dizziness, drowsiness, diarrhea or constipation, fatigue, memory or concentration problems, and a dry mouth or changed sense of taste. These reactions are usually mild to moderate and resolve after the initial titration period. Sativex is not recommended for pregnant women and people under 18 years old, or those with a history of **psychotic conditions**.

Sativex is approved for treatment of MS-related spasticity in Canada, New Zealand, and several European countries. The therapy’s approval abroad was supported by data from three Phase 3 clinical trials.

**Research supporting Sativex’s approval in Europe:**

<table>
<thead>
<tr>
<th>Year</th>
<th>Description</th>
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<tr>
<td>2007</td>
<td>Investigators concluded that cannabis-based medicine may represent a useful new agent for the treatment of MS spasticity.</td>
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<tr>
<td>2011</td>
<td>Researchers demonstrated the efficacy and safety of Sativex for treating MS spasticity.</td>
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<tr>
<td>2018</td>
<td>Results showed add-on Sativex provided better relief of resistant MS spasticity compared to antispasticity medication alone.</td>
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Recent research in Europe has revealed more about Sativex’s effectiveness and side effect profile post-approval. Investigators in Italy looked at 1,597 people with MS who had started treatment with Sativex for spasticity. They found that 23% of participants stopped treatment because it wasn’t effective and 16% because of side effects. The most common side effects were cognitive and psychiatric effects, fatigue and drowsiness. The researchers concluded that the first six weeks of treatment are useful in identifying those individuals in which Sativex could be effective. Another study analyzed data from 941 people with MS who were prescribed Sativex in the UK, Germany and Switzerland. Results show approximately 80% of participants benefitted from treatment and 30% stopped treatment because of lack of effectiveness or side effects. The most common side effects were dizziness and fatigue, and people were more likely to experience these during the first month of treatment.

Scientists have also looked at using Sativex to treat other MS symptoms. For example:

- **2010**
  Although their findings were not statistically significant, investigators in the UK and Belgium concluded that Sativex treatment improved bladder dysfunction.

- **2018**
  Italian researchers found Sativex treatment significantly reduced pain and abnormal cold perception in people with MS.

A Phase 3 clinical trial is underway in the United States to demonstrate the effectiveness of Sativex, compared with placebo, in the treatment of muscle spasms associated with MS. The estimated completion date for this study is February 2023. Investigators expect to enroll about 446 adults with MS and spasticity at 28 study locations across the United States, the Czech Republic, Poland and the United Kingdom. Participants will be
randomly assigned to either Sativex treatment or a placebo, both self-administered twice daily as an oral spray in addition to standard of care. Participants will record their daily number of muscle spasms in an electronic diary. The study will have three phases: a 4-week “baseline” period to establish a reference point, a 12-week treatment period (a 2-week titration phase and 10 weeks at the optimum dose), followed by a 2 weeks of follow-up evaluations, for a total of 18 weeks. Investigators will evaluate changes from baseline in participants’ average daily spasm count and Multiple Sclerosis Spasticity Score (MSSS-88), among other parameters. Future clinical trials are planned to further assess the drug’s effectiveness at reducing muscle spasm frequency and treating increased muscle tone. Researchers are hopeful that these trials will pave the way for FDA approval of Sativex for the treatment of MS spasticity in the United States.

Researchers are working to better understand the benefits and potential risks of cannabis as a treatment for MS and its symptoms. iConquerMS was developed to engage people with MS to drive and shape research on topics like this that are of great interest to the MS community. The data provided by network members are a valuable resource, giving investigators insight into the effectiveness of MS treatments, both from the clinical and personal perspectives. If you haven’t already done so, please consider joining. With your participation and support, we can add to the pool of real-world data that researchers have to draw from for these important studies and help improve quality of life for everyone living with the disease.

You know your MS better than anyone
Take surveys about your daily experiences and symptoms to help create a large pool of data for multiple sclerosis researchers.

BE PART OF THE CURE  Learn More At iConquerMS.org  iConquerMS
Welcome to the Team, Mark!

We are delighted to introduce you to Mark Gilliland, ACP’s newest Program Manager! Mark joined the ACP team in June and brings with him a background in data analytics, data visualization and automation solutions. We, at ACP, believe that research is the only way to greatly improve the outlook for people with MS and one day find a cure. Data collection, curation and sharing are key in the research process. The ACP Repository and iConquerMS are important tools for obtaining the necessary data to understand not only the causes of MS, but also the full scope of impact the disease has on those living with it. Mark’s expertise will be instrumental in managing the wealth of existing data in these databases, developing data collection mechanisms for new studies through iConquerMS and many other essential tasks.

Mark has six years of experience as a data professional. He primarily worked in public education alongside teachers and administrators, giving them access to academic data to allow them to make informed decisions about their instructional programs. He played an instrumental role in the transition to remote learning within his school system at the beginning of the pandemic by building automated systems to deliver curriculum and resources directly to students and track attendance. Mark also provided data analytics consulting services to a performing arts organization. He examined social media data to help them understand their audience and develop marketing strategies for a feature film. When asked what he enjoys most about being a data professional, Mark shares, “I enjoy seeing the impact that my work has on organizations. As a data professional, you can often see very quickly how the work you are doing is influencing and changing programs, strategies and actions. Being able to support non-profits is also something I find incredibly rewarding.”

Mark was born and raised in California and currently lives in Los Angeles. He attended the University of California Santa Cruz, where he earned a Bachelor of Arts in Economics. He is bilingual through self-study. In his words, “I speak Spanish fluently, initially taking classes in high school and practicing speaking with coworkers in Los Angeles, as well as from many trips to Mexico and Spain, reading books (starting with children’s books and eventually graduating to novels), watching movies, listening to music, and
making friends that speak Spanish… I would love to learn another language and have started studying Portuguese.”

When not at work, Mark enjoys being outdoors and staying fit. His favorite leisure activities include hiking, mountain biking, yoga, working out at the gym and going to the beach. He recently completed his open water diving certification and has completed several ocean dives and Cenote dives off the Yucatán peninsula in Mexico. Mark loves to travel. In his words, “My favorite destination so far has to be Japan. Everything that I ate while there was so incredibly delicious. The day I arrived in Japan, my phone decided to stop working, so I ended up having an old-school style trip exploring the country completely disconnected. I bought a Casio watch, a little notebook and pen, and some maps. It was amazing and very different from my usual trips where I always have Google Maps, Uber, Whatsapp, etc…. One of my favorite things to do in Tokyo was to buy a day pass for the train and get off at random stations, walking in random directions and discovering interesting business, restaurants, and local sights, then getting back on the train and doing it again at the next stop.”

Mark has a close friend that was diagnosed with MS several years ago. He first learned about ACP from the job posting for his current position. When asked what he finds most inspiring about ACP’s mission, Mark shares, “The focus on empowering patients and people by putting them at the center of the work, collaborating with them to build studies, programs, and systems…I am hopeful that my data skills will help to support the experts we work with and the patients we support to be more effective and efficient with how we use data to develop programs, studies, and initiatives.”

ACP was recently awarded funding for a project that involves mapping out the “MS patient journey” in order to more effectively engage them in research. Mark will be managing the development of this activity. The needs and priorities of a person living with MS change throughout their MS journey and are affected by many factors. Most outreach efforts for research are developed as “one size fits all” and, as a result, may fail to resonate with some individuals. Meeting a person where they are in their journey with the disease and providing them with tailored information about research participation is likely to be more
effective at increasing research participation. Working in collaboration with people affected by MS and other collaborators, Mark will help map the MS patient journey, focusing on research-related needs and interests and how they evolve, and also considering other factors such as age, gender, race and ethnicity. The team will then develop resources to engage people affected by MS in research based on where they are in their journey.

According to John Maxwell, “Teams are incredible things. No task is too great, no accomplishment too grand, no dream too far-fetched for a team. It takes teamwork to make the dream work.” We are excited to have Mark join the ACP team, lending his expertise and insight in ACP’s activities and look forward to what we will accomplish as we collaborate with people living with MS, researchers, healthcare providers, and other advocacy organizations (among others) and work together to accelerate MS research toward better ways to diagnose, treat and eventually cure the disease. Stay tuned!
July 2022 iConquerMS Spotlight

Don’t miss our Chat with Chat webinar series!

Hosted by our research collaborator Chat Ngorsuraches, the Chat with Chat webinar series provides a glimpse at the researchers working with iConquerMS, what they study, and how their work will benefit people with MS. In case you missed (or would like to revisit) any past episodes, here is a summary of the topics that have been covered to date:

In **Episode 1**, Chat spoke about his own research. He looked at various attributes of MS disease modifying therapies (DMTs) and found that neurologists and people with MS rank their importance differently. Tune in to hear the details!

In **Episode 2**, Chat spoke with Dr. Nina Bozinov about factors that affect quality of life for people with MS. Her research shows that things like increased disability, insurance type, living alone and a person’s gender affect wellbeing in both positive and negative ways. Want to learn more? Take a moment to share in the conversation!
In **Episode 3**, Chat spoke with Dr. Farrah Mateen about what we've learned about COVID-19 and MS. Even though less than 1% of iConquerMS members reporting having had COVID-19, the virus still had a high impact on health behaviors, MS care access, use of DMTs, employment and all aspects of social life. These findings are just a click away!

In **Episode 4**, Chat spoke with Dr. Farren Briggs about COVID-19 vaccine safety. iConquerMS data shows the Pfizer and Moderna vaccines were both effective in preventing COVID-19 symptoms in people with MS. Vaccination also reduced the chance of hospitalization and death from COVID-19. Click here for more information!

In **Episode 5**, Special guest Hollie Schmidt spoke with Dr. Mitch Wallin about telemedicine and MS. Dr. Wallin shared evidence that telemedicine provided a safe, easily accessible way to provide care for people with MS during the pandemic. However, it also had limitations. Are you curious what they were? Join in the discussion!

In **Episode 6**, Chat spoke with Annabel Decamps from Icometrix, a company that develops software and services that help people view, store, and analyze medical images such as MRIs. Icometrix surveyed the iConquerMS community about access to their own MRI files. This presentation summarized results from this survey. Listen in to learn more!

A heartfelt thank you to Chat and his colleagues for making this educational resource possible. Stay tuned for future episodes!
July 2022 Research Spotlight

RESEARCH OPPORTUNITIES

Research opportunity information may be provided on behalf of an external organization. Please refer to the contact information within each listing to identify the contact for questions or comments.

You are invited to participate in a research study comparing the effects of three diets!

You are invited to participate in a research study comparing the effects of three diets – the modified Paleolithic diet (elimination of gluten, dairy, and eggs), a Time Restricted Olive Oil-based Ketogenic diet or your usual diet with information about the USDA Dietary Guidelines for Americans. Participants in the usual diet group will be encouraged but not required to follow the Dietary Guidelines for Americans diet. Quality of life, fatigue, mood, and disease activity will be assessed by online surveys, study participant tasks, & brain imaging. The study will be held at the University of Iowa Hospitals & Clinics over two years. It will consist of three visits to Iowa City, month 0, month 3, & month 24. Each visit can last approximately three and up to six hours.

What you will be asked to do at home while on your assigned study diet

- Follow one of the three study diets randomly assigned to you for 24 months
- Report changes in health and medications
- Eat more non-starchy vegetables
- Eat more home-cooked meals
• Take recommended dietary supplements
• Complete daily food logs (three questions) on a smart phone
• If you are assigned to the ketogenic diet, you must take a blood ketone measurement daily for the first month and then twice a week for the rest of the study
• Complete online surveys
• Watch videos, review study diet guides and meet via Zoom to learn your assigned study diet
• Attend optional online support groups

What you will be asked to do at each of three visits to UIHC

• Complete fasting blood draws
• Complete physical motor skills, cognitive assessment and visual function tasks
• Receive a non-contrast MRI brain scan at first and final end of study UIHC visit (Month 0 and 24)

Requirements to participate

• Diagnosis of relapsing remitting multiple sclerosis (RRMS)
• 18-70 years old
• Able to walk 25 feet without support or unilateral support
• Willingness to adopt any of the three study diets, including the control diet
• Willingness to share medical records for the two years of the study
• Do not have heart disease, liver disease, kidney disease, or type 1 diabetes
• Do not have serious psychiatric disease that would make adopting a study diet more difficult
• Are not taking insulin or coumadin
• Have a smart phone, tablet or iPad to download a free app
• Have access to high-speed internet and a computer or smart phone to participate in video conferences via Zoom and complete online patient surveys
• Commitment to completing surveys for two years and attending the end of study visit
COMMON QUESTIONS

Do I need to live within a specific mile radius of Iowa City?

No, however, if travel funds are needed, we may be able to help. We can offer a travel stipend to support some travel expenses to and from Iowa City. Please speak with us about your needs. We also offer stipends to participants for attending the site visits and for completing the required online surveys.

Can I pick the diet I want to follow?

We ask that you follow the diet assigned to you. If following your assigned diet becomes difficult contact the study team for assistance.

Can I be in the study if I am in another MS-related study?

If you are in an interventional study investigating drugs, exercise, or other wellness behaviors you cannot be in this study. If you are in an observation-only study, you can still be in this study if you are willing to follow any of the three diets.

If you’re interested in taking our screening survey, please visit the link below or scan the QR code with your phone:
⇒ https://redcap.icts.uiowa.edu/redcap/surveys/?s=JX73EYRJNP9MHRR

If you have questions, please contact us at
⇒ MSDietStudy@healthcare.uiowa.edu
The University of North Texas Department of Kinesiology, Health Promotion, and Recreation is conducting a Research Study on Physical Activity Among Hispanic Persons with Multiple Sclerosis

The research will take place online.

You may be eligible if:

- You are over the age of 18
- You have been diagnosed with multiple sclerosis
- You identify as Hispanic/Latino
- You speak English or Spanish as a primary language

You may qualify to participate in a research study examining physical activity thoughts and behavior in Hispanic adults with multiple sclerosis.

Participation in the study includes one online survey that will be completed in 20-30 minutes. Participation is voluntary. You will receive compensation after completing the survey if you provide an e-mail address.

Please use the link below to complete the survey and contact the Principal Investigator with any questions using the study title “Theoretical Correlates of Exercise Behavior Among Hispanics with MS” Stephanie L. Silveira Stephanie.silveira@unt.edu

Survey Link: https://unt.az1.qualtrics.com/jfe/form/SV_1SogD4QwBBuvEc6
Help Us Make Strides in MS Research!

Who Are We?

MedRhythms is a digital therapeutics company that uses music to improve walking.

How Can You Help?

We are developing a device for individuals with multiple sclerosis to improve mobility. We are seeking volunteers with MS to walk with the product and provide feedback.

Interested?

Please email AppliedResearch@medrhythms.com or call (207) 370-2812 to learn more!
Would you like to contribute to MS research?
Do you seek new knowledge about MS and lifestyle?
Sign up now!

Developed at the University of Melbourne this online educational course aims to improve the health and wellbeing of people with MS.

What is involved for you?

- Completing an online survey before the course.
- Undertaking a free 6-week online course in your own time, taking 1-2 hours each week.
- Completing follow-up online surveys after course completion.

To sign up contact us now!

neu-research@unimelb.edu.au       msonlinecourse.com.au
Are you a mother with Multiple Sclerosis?  
If so, we would love your participation!!

**Why:** We are Occupational Therapy students who are conducting a research study to better understand the different components of parenting among mothers with Multiple Sclerosis

**What:** 30-minute survey

**Who:** Mothers with Multiple Sclerosis age 18 years or older, with child(ren) 40 years or younger

For more information about this study, please reach out!

Secure Email: csudh.otmothering@protonmail.com
A study looking at language usage among people with disabilities – all adults with disabilities are welcome to participate!

What is the study about?

This research attempts to gather evidence on the preference between identity-first and person-first language by and for people with disabilities. The lead researcher is a graduate student in the University of Washington’s department of Computer Science and Engineering as a member of multiple labs focused on accessibility in computing.

Why participate?

The topic of language preference has been discussed often, but often while excluding community and individual perspectives. The research data gathered will help to work towards more consistent respectful language usage in future projects. Participants will contribute to a public website that features a visualization that explores the ways different backgrounds (age, country, gender) may or may not affect language preference.

Who can participate?

All people with disabilities over the age of 18 who have access to and can use a computer and access to the internet are welcome to participate.

How to participate:

Follow this link: https://bit.ly/disability-language-survey to access our participant survey. It should take around 5 minutes to complete.
A new topic for the Our Questions Have Power program!

When it comes to MS symptoms and how to manage them, what questions are most important to you? What symptom-related topics do you wish researchers were studying? Your questions are valuable and we invite you to share them through the Our Questions Have Power program on the iConquerMS website.

The Our Questions Have Power program was launched in March 2021 with an initial focus on COVID-19. Questions submitted by iConquerMS members have helped shape the COVER-MS vaccination study and are being shared with the research community to guide other efforts.

We’re now extending Our Questions Have Power to include a second topic: MS symptoms and their management and treatment. As before, you’re invited to share questions on this topic that you think should be studied and to vote on questions submitted by other iConquerMS members. We’ll share these questions with people affected by MS, researchers, healthcare professionals, advocates, and funders – and, together, we’ll work to launch research studies to answer those questions.

It’s easy to share your ideas and input in Our Questions Have Power!

Log in to iConquerMS to start (create an account first if you don’t already have one).

Click PROPOSE an MS Research Question to submit a question you’d like to see studied.

Click VOTE and COMMENT on MS Research Questions to review, comment, and vote on questions submitted by other iConquerMS members.