The effects of 3FDC dietary supplementation on psychological functioning in an adult population

INFORMATION SHEET

STUDY PROTOCOL ID: FDC001

HUMAN RESEARCH ETHICS COMMITTEE NUMBER 2020_014

INTRODUCTION

Each year CSIRO perform a number of research projects involving human participants. We examine the effect of different diets, nutrients, and supplements on diseases and various aspects of our health.

In this study we are interested in learning about how a recently developed dietary supplement may change how people feel. This supplement is called 3FDC and it is developed by an Australian company called Anatara Lifesciences as part of their **Ga**strointestinal **R**e-**P**rogramming (GaRP) complementary medicine product.

3FDC is made of three active ingredients: Sodium Butyrate, L-threonine, and Vitamin D3. Although these ingredients have been used in people previously and are already known to have broad-ranging effects on our gut and body, the combined effect of these ingredients has not been studied yet. It's believed the combined effect of these ingredients may include changing how people feel in a positive way through a link between the gut and the brain known as the gut-brain axis. This study will help us understand if consuming the 3FDC supplement will lead to improvements in how people with moderate depression, anxiety, or stress feel.

This study is being paid for by Anatara Lifesciences.

WHAT IS THE AIM OF THIS STUDY?

The primary aim of this study is to evaluate the effectiveness of daily consumption of the Anatara Lifesciences 3FDC dietary supplement on how people with moderate levels of depression, anxiety, or stress feel.

HOW WILL THIS STUDY BE CARRIED OUT?

WHO CAN PARTICIPATE?

To be eligible to take part in this research, there are a few criteria you must meet. Have a look through the criteria below. If you feel this describes you, and you are keen to take part, then please complete the Recruitment Questionnaire and return it to us. If you are unsure or have any questions, do not hesitate to contact the clinic for assistance, either by phone 8305 0615 or email CRUstudies@csiro.au

Key eligibility criteria:

1. Access to a smartphone and willing to download a free application from the app store
2. Able to access own email address
3. Male or female individuals
4. Aged between ≥18 & <56 years
5. Body mass index ≥18.5 and ≤35 kg/m^2 (we can calculate this for you)
6. Have not experienced a previous adverse reaction to cellulose
7. Not currently taking any of the following supplements:
    - Supplements containing prebiotics or probiotics
    - Fibre supplements (e.g., psyllium plant sterols, Metamucil, Benefibre)

8. Not currently taking any of the following types of prescribed medications:
    - Antidepressants
    - Anxiolytics
    - Narcotics
    - Stimulants
    - Anti-psychotics
    - Antibiotics
    - Systemic steroids (e.g. prednisolone)
    - Chronic drug therapy that interferes with vitamin D metabolism, such as glucocorticoids (e.g. dexamethasone)
9. Not currently participating in psychological therapy with a mental health clinician (including, but not limited to: psychologist, counsellor, GP etc)
10. Not currently doing nightshift work
11. Do not have a significant acute or chronic illness (i.e., psychiatric, gastrointestinal, cardiovascular [except uncontrolled hypertension], endocrine or immunological)
12. Have not experienced a cardiovascular event such as congestive heart failure, heart attack, stroke, or angina (chest pain) in the past 3 months
13. Do not currently have, or have a history of, inflammatory bowel disease (e.g., ulcerative colitis, Crohn's disease)
14. Have not had previous brain, heart (e.g., coronary artery bypass surgery), or gastrointestinal surgery
15. No current or planned hospitalisations that will take place during the study period
16. No participation in a clinical study within the last month
17. Willing to attend two visits at our clinic at SAHMRI (Baseline and 6 weeks)
18. Willing to consume the study supplement daily for a period of 6 weeks
19. No history of smoking/vaping within the last 6 months
20. Not currently pregnant or lactating
21. Blood haematology and biochemistry test results within the normal reference range at screening

WHAT IS GOING TO HAPPEN AND WHAT TESTS WILL BE DONE?

After you have read and had time to consider the information contained in this information sheet, and if you decide to take part in this study, you will be asked to complete a screening questionnaire to ensure that you fit the criteria of the study. You will also be asked to provide information on your medical history and current medication/supplement use.

Based on these details provided by you, you may be contacted by telephone and/or email and invited to undergo a telephone screening assessment. You will be asked to answer some questions including about how you feel using a questionnaire called the Depression, Anxiety and Stress Scale. The purpose of this assessment is to make sure you are eligible for the study, and it does not necessarily mean that you will be able to take part.

If you are deemed eligible, you will then be invited to attend an in-clinic screening visit in person at the CSIRO Nutrition Research Clinic at the South Australian Health & Medical Research Institute (SAHMRI), located on North Terrace in Adelaide. At this visit, you will be asked to sign a formal consent form. We will assess your general health status and vital signs. This will include the assessment of your temperature, body weight, height, blood pressure, respiratory rate, and heart rate. We will also review your medical and surgical history and your current medication/supplement use. You will also be asked to provide a urine sample (if you are female and of childbearing potential) to confirm you are not currently pregnant. We will also collect a blood sample.

We will work with you to plan a suitable appointment schedule for the remainder of the study. At any time, you will have the opportunity to ask questions you may have of the research team whether by email, phone or in person. We will notify your GP of your participation in this trial and any medically relevant incidental findings that may require following up over the course of the study. If this occurs, you will also be informed.

STUDY VISITS:

Over the course of the study, you will be required to attend the CSIRO Nutrition Research Clinic at SAHMRI, North Terrace, Adelaide on 2 occasions and you will be asked to complete either an online questionnaire on 8 other occasions, or you may

choose to download our CSIRO CODE+PRO app. We will discuss these options with you at your clinic appointment. You will complete a 6-week supplementation period, with a clinic visit immediately before and after this period.

At each clinic visit, the following information and assessments will be collected:

ASSESSMENTS	**MONTH**	**1**	**1**	**2**	**2**	**3**	**3**
	Visit type	phone	**CLINIC**	**CLINIC**	online	online	**CLINIC**
	Duration (approximate minutes)	**15**	**45**	**90**	20	**20**	90
	Medical and surgical history (by questionnaire & interview), medication review, height/weight		X	X			X
	Body weight measurement and vital signs		X	X			X
	Blood sample (health and nutritional markers)		X	X			X
	Questionnaires (psychological and gut health)	X		X	X	X	X
	Dietary intake (weighed food diary for 3 days)				X	X	
	Product compliance and medication use	**2 minutes daily via a mobile app or 10 minute weekly online survey**					

You will be randomly assigned to receive either the Anatara Lifesciences 3FDC supplement or placebo (a control dietary supplement). You have a 50% chance of receiving the Anatara Lifesciences 3FDC supplement and a 50% chance of receiving the placebo. The Anatara Lifesciences 3FDC supplement and placebo will be identical in appearance and neither you nor the clinic staff will know what treatment you have been assigned. You will be given your supplements at your first study visit. You will need to take the supplement with a liquid (e.g., water or juice) once in the morning and once in the evening (twice per day in total) every day for the duration of the 6-week intervention period. You will be asked to complete a daily log via a mobile app or a paper-based diary to record your supplement intake and any other medications you take. The logs will take about 10 minutes to complete each week.

During the week before your baseline visit and the last week of taking the supplement, you will also be asked to complete a food diary on a mobile app called Research Food Diary on three separate days. The food diary will take approximately 15 minutes to complete each day. The clinic staff will tell you on which days to complete the diaries.

After two weeks and again after four weeks of treatment you will be asked to complete the following questionnaires via an online survey link:

- Depression, Anxiety and Stress Scale
- The Hospital Anxiety and Depression Scale
- Perceived Stress Scale
- Warwick Edinburgh Mental Wellbeing Scale
- Penn State Worry Questionnaire
- Gut Symptoms Rating scale

In total, these surveys will take between 15-25 minutes to complete.

It is important to tell the study staff about any treatments or medications you may be taking, including over-the-counter medications, vitamins or herbal remedies or other alternative treatments. We will ask you to otherwise maintain your habitual lifestyle habits, including physical activity levels and dietary intake. If you are prescribed medication or any changes to medication by your doctor, we ask that you keep a record of the type, dosage and purpose of medication used and inform the study team in a timely manner. The study Medical Doctor will determine the best course of action should your GP prescribes you with such medication, which may include withdrawing you from the study. We will also ask you about any side effects that you may experience throughout the study.

At the completion of the study you will be provided with a $140 payment to thank you for your time taken to participate in this research project and to cover any expenses that you may experience. Should you withdraw before completion of the trial, reimbursement will be calculated on a pro rata basis for the study activities that you have completed.

WHAT ARE THE BENEFITS OF PARTICIPATING IN THIS STUDY?

You may not benefit directly from participation in this study, but you will be providing a valuable contribution to the scientific knowledge in this field.

ARE THERE ANY RISKS INVOLVED?

Anatara Lifesciences 3FDC is a new dietary supplement not currently approved for use or available for purchase within Australia. Although the individual components are recognised as generally safe for human consumption, it is possible that adverse events could occur from the mixture of the components together.

There have been no known reported serious side effects associated with any of the individual ingredients contained within this product, however you should report your medical history and any medication use to research staff as there is a chance that the ingredients may interact with certain conditions and medications.

There may also be some risks in adhering to the study protocol:

There is a small risk of infection/blood clotting and or bruising following blood collection, however this is minimised by having the blood samples collected by trained phlebotomist/nurses.

Anatara Lifesciences 3FDC is not suitable for individuals who are allergic or hypersensitive to cellulose. We encourage you to consult your health care professional regarding any potential allergies or sensitivities you may have to this ingredient.

POTENTIAL RISKS TO THE UNBORN CHILD & NEWBORN BABIES

The 3FDC dietary supplement is a mixture of three active components: sodium butyrate, L-threonine, and cholecalciferol (vitamin D3), in the form of minitablets. The components are natural active ingredients and previous human studies have demonstrated them to be safe.

However, the effects of 3FDC on fertility, including future fertility, on the unborn child and on the newborn baby have not been studied and are not fully understood. Because of this, it is important that you are not pregnant or breast-feeding and do not become pregnant during the course of the study. You must not participate in the study if you are pregnant or trying to become pregnant, or breast-feeding. If childbearing is a possibility, you will be required to undergo a pregnancy test prior to commencing the study and at each clinic study visit.

You must use effective contraception over the course of the study and for a period of one month after completion of the study. You will discuss methods of effective contraception with clinic study staff. If you do become pregnant whilst participating in the study, you should advise the clinic study staff immediately. You will be withdrawn from the study and advised on further medical attention should this be necessary. You must not continue in the study if you become pregnant. You will be followed up for the duration of your pregnancy and the status of both yourself and your newborn will be documented and made available to the Study Investigators and Sponsor.

Participants with partners of childbearing potential must inform their partner of their clinical trial participation and use adequate protection for the duration of their participation in the clinical trial. Partners of childbearing potential should consider the use of effective methods of contraception over this time. Participants should refrain from the donation of sperm for the duration of the clinical trial participation.

There may be side effects that the researchers do not expect or do not know about. You should tell the study staff about any new or unusual symptoms that you experience.

During the study, new information about the risks and benefits of the project may become known to the researchers. If this occurs, you will be told about this new information and the study doctor will discuss whether this new information affects you and your participation.

All human research undertaken by the CSIRO must comply with the values, principles, governance and review process specified in the NH&MRC National Statement on Ethical Conduct in Human Research (2007). A copy of the National

Statement can be found at https://nhmrc.gov.au/research-policy/ethics/national-statement-ethical-conduct-human-research .

If you were to suffer an injury as part of your participation in this project, the pharmaceutical industry has set up a compensation process with which the Sponsor of the research, Anatara Lifesciences Pty Ltd, has agreed to comply. Details of the process and conditions are set out in the Medicines Australia Guidelines for Compensation for Injury Resulting from Participation in a Company-Sponsored Clinical Trial. We would recommend that you seek independent legal advice if such circumstances were to arise.

ALTERNATIVES TO PARTICIPATION.

Participation in this research is voluntary and is not your only option. Given the nature of this research, you may wish to make a personal appointment to discuss the appropriateness of this research study for you with your usual GP or healthcare practitioner, who has knowledge of your medical history, prior to deciding whether or not to take part in this research project.

WHAT IF I WISH TO WITHDRAW?

You are free to withdraw at any time during the study, without penalty. However, subject to any relevant legislation and depending on the date of publication, it may not be reasonable or practical to remove your information. Information collected up to the point of your withdrawal, including any blood samples, will be included in the analysis of the study data, unless you request that they be withdrawn. Where you would like to withdraw your consent, please contact the clinic via CRUstudies@csiro.au.

It is also important to understand that we may choose to end your participation. That decision may be made if we decide that the study is not in your best interest, if you are unable to follow the protocol of the study, or if the study is discontinued. If we have to end your participation, we will make sure you are made aware of the reasons.

The information that CSIRO gathers from you for the purpose of this study will be maintained for the duration of this study and for up to fifteen years after the study. At the completion of the study (or within 15 years following the completion of the study) your information will be destroyed or permanently de-identified, subject to any legislative requirements. Some of the blood samples collected during the course of the study will be stored for future analysis depending on the results obtained for up to 2 years before disposal.

YOUR OBLIGATIONS AS A PARTICIPANT.

You will need to inform a study staff member of any changes in your health as some changes could have an effect on your participation in the study and the study findings. You must also be able to undertake all relevant procedures during the study period.

HOW WILL MY PRIVACY BE PROTECTED?

Your personal information is protected by the *Privacy Act 1988* (Cth) and CSIRO will handle your personal information in accordance with this Act and the NH&MRC National Statement on Ethical Conduct in Human Research (2007, updated 2018).

CSIRO is collecting any personal information and sensitive information (including health information) you provide to us, or to a third party in relation to this study, for the purposes of the study and related scientific research. If you do not provide your personal information, you will not be able to participate in this study.

Where you provide the personal or sensitive information of third parties to CSIRO, including your emergency contact and your relatives, you must have consent from these individuals to do so. Where you do not have consent, please do not provide this information.

CSIRO will disclose your personal information to third parties, including Clinpath Pathology and Xyris for the above purposes. With your consent, CSIRO will also notify your doctor of any medical condition deemed significant by the Clinical Research Unit Medical Officer. CSIRO will also disclose de-identified and/or aggregated information to Anatara Lifesciences, the ethics board for this study, regulatory bodies and other health professionals for the purposes outlined above.

Study results will be de-identified and/or aggregated and published in a variety of forums including research publications and press releases. A de-identified summary report will also be mailed to you.

You will be asked to download the Research Food Diary application, which is developed by Xyris Software. Upon registering for the Research Food Diary application, you will be agreeing with the developer's privacy policy for the handling of your personal information. Xyris uses cloud services located in Australia,however, Xyris also uses third-party contractors, contracted service providers and customers with whom Xyris has a business association, with servers based overseas. This means your personal information may be transferred outside of Australia. By downloading and using the Research Food Diary App, you consent to the transfer of your personal information outside of Australia and acknowledge that this information may not be subject to the requirements of the Privayc Act. For more information, please review Xyris' Terms and Conditions and Privacy policy here: https://support.xyris.com.au/hc/en-us/articles/206596013-Privacy-Policy

We will not use or disclose your information for direct marketing purposes.

The CSIRO Privacy Policy available at https://www.csiro.au/en/About/Access-to-information/Privacy outlines how your personal information will be handled, including details about how you can seek access or correction of the personal information we hold about you, how you can make a complaint about a breach of the Australian Privacy Principles (APPs) and how CSIRO will deal with the complaint. If you require further information on how your personal information will be handled please contact privacy@csiro.au .

IF YOU HAVE FURTHER QUESTIONS.

Please call the Nutrition Research Clinic on 8305 0615 or via email CRUstudies@csiro.au. Please mention that you are calling regarding the 3FDC dietary supplement Study.

This study has been approved by the CSIRO Human Research Ethics Committee. If you would like to speak with someone with respect to ethical matters or wish to register a formal complaint about the conduct of this research, please contact the Secretary of the Committee via email at chmhrec@csiro.au or phone on (07) 3833 5693.

CONSENT

I agree to the collection, use and disclosure of my personal information, including my sensitive information, in the ways described in the Participant Information Sheet entitled "**The effects of 3FDC dietary supplementation on psychological functioning in an adult population".**

I agree to the transfer of my personal information, including my sensitive information, to Xyris servers located overseas. I acknowledge that this information may not be subject to the requirements of the Privacy Act.

Where I am asked questions about individuals other than myself, I confirm that I will obtain those individuals' consent to share their personal information, including their sensitive information, with CSIRO prior to sharing their information with CSIRO.

Full name: …… Signature: …… Date: / /

CONTACT US

CSIRO Nutrition & Health Research Clinic

SAHMRI North Tce, Adelaide SA 5000

PO Box 10097, Adelaide SA 5000

T (08) 8305 0615 1800 850 036 • ABN 41 687 119 230

As Australia's national science agency and innovation catalyst, CSIRO is solving the greatest challenges through innovative science and technology.

CSIRO. Unlocking a better future for everyone