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1) Introduction

More than 50% of individuals over the age of 45 are living with diet-related noncommunicable health conditions, placing a significant burden on NHS resources [National Food Strategy, Ch.16, 2021]. Addressing this growing public health challenge requires the development of foods with enhanced nutritional value. Functional ingredients that support health and well-being are essential not only for improving individual health outcomes but also for promoting a healthier planet.

In this context, BioMara and Aberystwyth University (AU) are collaborating to evaluate the health benefits of fucoidan, a seaweed-derived bioactive polysaccharide, in human clinical trials. Fucoidan has demonstrated a wide range of biological activities, including anticancer, antioxidant, immunoregulatory, antiviral, and anti-inflammatory properties [Cardoso, 2014; Fitton, 2015].

While in vitro and animal studies have shown fucoidan's potential to reduce colitis [Lean, 2015; Liu, 2022], evidence from human trials remains limited. To date, only two studies have investigated its effects in humans: one examining fucoidan combined with wheat for its impact on gastritis [Kan, 2020], and another assessing its potential in managing chronic colitis [Ye, 2024].

This study aims to conduct a randomised, placebo-controlled, parallel-group human trial to assess the potential effects of spray-dried fucoidan on gastrointestinal (GI) symptoms, general health, well-being, and dietary patterns in young adults. The study will rely on self-reported data to evaluate these outcomes.

We are aiming to recruit a cohort (n = 30) where volunteers (F/M balanced, young adults 18-35y, n = 15/treatment group) will consume either spray dried fucoidan (250mg in vegan clear capsules) or placebo (Microcrystalline cellulose) control daily for 28-d and access fucoidan on gastrointestinal(GI) symptoms, health and well-being, and associated diet.

This will be a remote trial where no biofluids are collected. Self-report questionnaires will be employed pre and post-trial on RedCap: Digestion-associated QOL Questionnaire (DQLQ), Short Form Health Survey SF-12 (SF-12), Bristol Stool Scale/Bristol Stool Chart, alongside general health and well-being questionnaires (e.g. General Health Questionnaire (GHQ-12), Warwick-Edinburgh Mental Well-being Scale (WEMWBS) and EQ-5D items (Health Survey for England) (collated in Appendix 1) and a Food Frequency Questionnaire.

This study will provide valuable insights into the potential of fucoidan as a functional food ingredient for improving gut health and overall well-being. The findings will contribute to the growing body of evidence supporting the role of bioactive compounds in addressing diet-related health conditions and informing future larger-scale clinical trials.

2) Statement of Purpose

A randomised, placebo-controlled, parallel-group human trial to assess the potential effects of spray-dried fucoidan on gastrointestinal (GI) symptoms, general health, well-being, and dietary patterns in young adults over 28 days. The study will rely on self-reported data to evaluate these outcomes.The placebo will be matched to the active product by taste and texture.

3) Investigational Product

Although fucoidan is derived from natural sources, participants will be informed of potential adverse effects, such as gastrointestinal discomfort and allergic reactions. The supplement is food-grade but is not currently available for sale in the UK. It is not presented for medicinal purposes and thus does not fall under the classification of a Clinical Trial of an Investigational Medicinal Product (CTIMP) as defined by the Medicines and Healthcare products Regulatory Agency (MHRA). Therefore, the study is subject only to general food regulations and complies with all relevant food safety standards.

Fucoidan is classified as a novel food in the United Kingdom and has been authorized for use under specific conditions. According to the Food Standards Agency's register of authorised novel foods, fucoidan extracted from *Fucus vesiculosus* is permitted for use in foods, including supplements, with a maximum daily intake of 250 mg.

Human studies involving fucoidan have been conducted previously, including research by Takahashi et al. (2018), Wright et al. (2018), Kan et al. (2019), and Ye et al. (2024). The supplements used in this study are vegan, produced, and stored in a food-grade facility to ensure the highest standards of safety and quality.

The supplements are suitable for vegetarians and vegans. The supplements are produced and stored in a food grade facility.

3.1) Quality

A comprehensive pesticide residue analysis was conducted by ALS (10/07/2023) on the fucoidan sample to ensure it meets safety and regulatory standards for consumption. The test screened for a wide range of commonly used agricultural pesticides, and the results indicate that all tested compounds were either not detected or were present in concentrations well below permissible limits. This confirms that the fucoidan product is free from harmful levels of pesticide contamination and is compliant with international safety guidelines.

3.2)Dose

Volunteers (F/M balanced, young adults 18-35y, n = 15/treatment group) will consume either spray dried fucoidan (250mg in vegan clear capsules) or placebo (Microcrystalline cellulose) control daily in the morning for 28-d.

4) Study Design

5.1) Objectives of the Study

5.1.1) Primary Outcome Measure:

Gastrointestinal health
Measured using: Digestion-Associated Quality of Life Questionnaire (DQLQ) and Bristol Stool Scale/Bristol Stool Chart
Time frame: Improvement in self-reported GI symptoms from baseline to 28 days post-intervention (fucoidan or placebo)

General Health and well-being
Measured using: Short Form Health Survey (SF-12), General Health Questionnaire (GHQ-12), EQ-5D items (Health Survey for England)
Time Frame: Improvement in self-reported general health from baseline to 28 days post-intervention)

Mental well-being
Measured using: Warwick-Edinburgh Mental Well-being Scale (WEMWBS)
Time frame: Increased mental well-being score from baseline to 28 days post-intervention

5.1.2) Secondary Outcome Measures:

Feasibility of fucoidan supplementation
Measured using: Participant compliance (daily intake tracking) and Completion rates of online questionnaires and diet diaries
Time frame: Across 28 days of intervention

Dietary patterns and food intake
Measured using: Diet via EPIC Food Frequency Questionnaire
Time frame: Change in reported dietary patterns from baseline to 28 days post-intervention

Variability in response to fucoidan
Measured using: Inter-individual variation in questionnaire outcomes (GI symptoms, mental well-being, general health)
Time frame: From baseline to 28 days post-intervention

5.2) Subject Selection

We are aiming to recruit a cohort (n = 30) where volunteers (F/M balanced, young adults 18-35y, n = 15/treatment group)

- **Inclusion Criteria:**

consenting adults >18 -35 y Age
Subjects able to provide written informed consent PRIOR to performing any study procedures.
Subjects who are able to commit to consuming daily supplements
Subjects who are willing to complete a series of online questionnaires

- **Exclusion Criteria:**

Serious health conditions that require daily long-term medications
Allergens: any participant with molluscs and crustacean allergens
Those taking anticoagulant and blood sugar-lowering medications
A history or current diabetes, or gut inflammation (Crohns, IBD)
Subjects with medical condition or disease that is life threatening
consume high dose of alcohol > 21 unit per week for men and > 14 units per week for women
food allergy /food intolerance/ eating disorder or are on a specially prescribed diet
pregnant or breast feeding
Subjects who smoke cigarettes or use other products containing nicotine
Subjects who are already regularly taking fucoidan or supplements related to fucoidan within 30 days of screening.

5.3) Study Design

Upon first point of contact, participants shall be provided with an information sheet detailing the study, followed by a REDCap link for completion of eligibility screening. This study is conducted remotely, and no

in-person visits to the Well-being and Health Assessment Research Unit (WARU) at Aberystwyth University are required unless specifically requested by the participant.

Online Eligibility Session

Provide basic details (name, DOB, gender, preferred contact method), and answer a few medical health questions, within REDCap (compliant with GDPR standards), to assess eligibility. *For participants without access to a valid email address or home PC, these details will be obtained over the phone with a member of the WARU team.*

Online/remote Induction Session

A consent form will be mailed to the participant. Upon signing and returning the consent form, participants will be asked to self-report their height, weight, waist, and hip measurements. Once the signed consent form is received and verified, study questionnaire links and supplements will be mailed to the participant.

Follow-up (28 Days Later) after consuming the supplement daily:

After 28 days, participants will be asked to repeat and submit their height, weight, waist, and hip measurements. Additionally, they will be required to complete follow-up questionnaires online.

Study materials:

All capsules and study materials will be prepared and securely stored at the Well-being and Health Assessment Research Unit (WARU) at Aberystwyth University.

6) Participant Risks

Fucoidan has already been tested for any adverse effects in a human cohort, however if any negative effects occur, the participants are asked to refrain from continuing in the study. Allergens: any participant with molluscs and crustacean allergens should not take part in the study.

Some of the questionnaires will require the participant to answer questions relating to their physical health, well-being and diet. They will not receive feedback on their questionnaire scores because they are NOT intended for diagnostic or clinical purposes. However, if they have any concerns regarding the scoring criteria, or about their health in general upon completing these questionnaires, then we recommend that they speak to their GP. If they have any questions regarding any of the questionnaires and how they are used, then they are to contact WARU at waru@aber.ac.uk. If they would like to speak to someone generally about their well-being and mental health, or if they have any other well-being health concerns, then we recommend that they use one of the support services listed at the end of the Participant Information document.

7) Benefits to participant

There will be a £20 voucher if they complete this study. They will allow researchers to gain important insight into fucoidan supplement to improve health and well-being in healthy volunteers, which may be applied to other cohorts such as those suffers suffering gastrointestinal issues.

8) Privacy/confidentiality

Participants are informed that only the researchers involved with the study will be able to look at the information they provide. Specific details and personal identifiers will only be available to the researchers. At the end of the study, any information relating to participants will be made

pseudonymous (coded without their name associated). Participants will not be identifiable in any publication that may arise from this research. Electronic files will be kept in a logical manner and will always be kept grouped within specific folders and password-protected. Files are backed up and all data storage is using the AU network. Data is collected directly into REDCap. However if paper versions are used, once the raw data has been extracted from a paper version onto a computer, the paper will be destroyed via a paper shredder or in confidential waste bags to ensure the participant's confidentiality. There may be times when keeping paper forms are necessary (consent forms), but in this case the paper versions will be kept in a locked filing cabinet. All files that are stored on the WARU share drive will always be protected with a secure password. Setting passwords will automatically encrypt the document and will not allow any unauthorised access to the data. The Gatekeeper of the passwords delivers the passwords by encrypted emails.

9) Safety Monitoring

If a participant, or a member of their family/household become unwell during the study, then they are pre-warned to alert a member of the research team immediately using the contact information they have been provided. Participation in the study will be suspended immediately until further discussion with the research team has taken place. If they become unwell at any point and need medical assistance, they are advised to contact 111 and seek advice from the NHS health sector or their doctor's surgery. We have a duty of care towards them and can help monitor their health remotely over 14 days and will help in any way we can.

10) Data analysis and statistics

Statistics will be conducted by the Aberystwyth University researchers.