A Mini Review on Biomarkers of Whole Grain Barley and Whole Grain Wheat Intake*

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Abstract

1 Introduction

Whole grains (WGs) and their processed food could have health beneficial effects. However, epidemiologic studies showed mixed results due to subjective self-report based food exposure measurement[1]. Using Biomarkers of Food Intake (BFIs) can potentially measure food exposure in population more objectively with accuracy and detail[2].

Alkylresorcinols (ARs) and their metabolites were widely reported and validated biomarkers for WGs intake. In plants commonly consumed for food, ARs only present high amounts in rye and wheat, especially concentrated in their bran parts[3]. Therefore, ARs have the possibility to be used as biomarkers for whole grain wheat and rye intake.

Increasing evidence showed that, different WG cereal types (such as wheat, rye, oat and barley etc.) could benefit health differently. However, classical self-reported measurement tools used in observational studies could cause a lot of deviations and confoundings to distinguish each cereal type. Therefore, discovering BFIs of each whole grain type could potentially provide a tool to accurately quantify their exposures.

This mini-review aimed at systematically examining available literatures to obtain information of potential biomarkers for WG barley and wheat. This will prioritize further identification and validation of the thesis work.

2 Materials and Methods

This review referred the 8-step systematic BFIs literature review guidelines[4]. The flowchart was included in Appendix (Fig-1)

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The objective of this literature review was to identify and evaluate reported potential biomarkers for dietary assessment for whole grain wheat and whole grain barley.

Keywords as suggested in the guidelines[4] were used to search in 3 database (PubMed, Web of Science, Scopus). Keywords used for searing BFI barley in human: (barley) AND (biomarker* OR marker* OR metabolite* OR biokinetics OR biotransformation OR pharmacokinetics) AND (intake OR meal OR diet OR ingestion OR consumption OR eating OR food) AND (human* OR men OR women OR patient* OR volunteer* OR participant*) AND (trail* or experiment OR study) AND (urine OR plasma OR blood OR serum OR excretion OR hair OR toenail OR faeces OR faecal water). The first element was changed to wheat for wheat biomarker searching.

Due to limited amount of searching results, barley searching scope was expanded to animal studies. Therefore, the keyword (animal* OR goat OR sheep OR cow OR mice OR mouse* OR animal model* OR dog*) was used to replace the previous subjects. In addition, 'feed' was added into intake element.

Other database including HMDB[5], FoodDB[6], PhenolExplorer[7], Dictionary of Food Compound[8] were also used.

3 Results

3.1 WG barley

The literature search got 129 records after removing duplicate records from merged 3 database search results. However, within them, none of the studies directly investigated WG barley intake biomarkers. This could be explained by limited dietary exposure of barley in population. Although barley is the 4th most produced cereal grains worldwidely. Most of them is used for brewing or feed. Only approximately 4% is consumed directly[9].

When the scope expanded to animal studies, the search results did not yield any direct research about BFIs. Most of studies were interested in how barley feed can benefit the growth of animal or quality improvement of animal-source product[**ISI:000272990200002z**, 10].

A 2-month intervention study[11] incorporated 75% refined drum wheat and 25% WG barley. The fecal samples showed significant change in microbiota and metabolome after intervention[11]. However, no specific metabolite can indicate WG barley intake.

ARs and their metabolites may not indicate WG barley intake. Several observation studies[12, 13] investigated correlation between ARs metabolites and whole grain intake. Although these studies tried to cover many whole grain species, for example, one study[13] listed 7 types of regularly consumed WGs in American populations in the FFQ (Food Frequency Questionnaire)[1], barley

[1]Dark breads, High-fiber or bran cereals, Cooked cereals and grits, Regular granola, Granola bars and cereal bars, Plain popcorn (no butter) or low-fat microwave popcorn, Buttered or gular microwave popcorn

was not solely listed. Therefore, although ARs and their metabolites got good correlation with these 'Whole-grain intake'. Readers should be cautious to apply them to WG barley. In addition, ARs concentration in cereal barley is much lower compared with WG wheat and rye, with similar concentration with refined wheat and rye flours (Table-1).

Cereal	Conc. range in cereal	Conc. average or range in WG flour	Conc. average in refined flour	Main homologues	C17:C21 homologues ratio
Rye	360-3200	972	90	C17, C19, C21	0.8-0.9
Wheat	761-8390	490-710	36	C19, C21	0.07-0.1
Barley	55.8-98.2	NA	NA	C19, C21, C25	NA

Table 1: Prensence of ARs in Cereal Grains, adapted from [14–16](unit: µg/g dm)

Most research results focused on barley's *effect biomarkers* as defined by Dragsted[17] and Gao[18], such as bowel health indicators, lipid profiles and cardiovascular disease (CVD) markers, etc.

Further search results in food chemistry, cereal science and plant science involved some compounds only present in barley other than other food. These could give hints for further identification. The results were summarized in Table-2.

To conclude, barley, especially WG barley attracted a lot of interest due to its health beneficial effects for chronic disease. However, due to barley's limited exposure, currently there's no biomarkers can indicate its intake. However, a lot of sparse information was reported from cereal and food chemistry could further benefit identification and validations of WG barley's intake biomarkers.

No	Candidate biomarker	Formula	Chemical group	Presence in Food	Reference
1	Hordenine	C10H15NO	alkaloid	germinating barley, beer and other plants	[19]
4	Hordatine A	C28H38N8O5	alkaloid	only reported in barley	FoodDB(002330)
4	Hordatine B	C29H40N8O5	alkaloid	only reported in barley	FoodDB(002328)
2	Distichonic acid A	C10H18N2O8	gamma amino acids and derivatives	only reported in barley	FoodDB(18164)
3	Distichonic acid B	C10H18N2O8	gamma amino acids and derivatives	only reported in barley	FoodDB(018165)
5	14,16-Nona cosanedione	C29H56O2	ketone	only reported in barley	FoodDB(013891)
6	N-Norgramine	C10H12N2	indole	only reported in barley	FoodDB(017815)

Table 2: Candidate Biomarkers for WG barley intake

3.2 WG wheat

The literature search got 312 results after removing duplicate records from merged results. XXX were used.

ARs and their metabolites were widely reported, validated and applied biomarkers for WG wheat and rye intake. Depending on different milling methods and grain species, ARs concentration varied in WG rye and wheat. In order to distinguish wheat and rye intake, the homologue ratio C17:0/C21:0 was proposed as an biomarker to indicate in dietary pattern which cereal dominates. if this ratio is close to 1.0, then rye dominated. If the ratio is close to 0.1, then wheat dominated[20].

Type of WG	No. subjects	Sample type	Analytical method	Candidate biomarker(s)	Reference
WG wheat WG rye	39	plasma	GC-MS	AR C17:0/C21:0	[20]

Table 3: Potential Biomarkers of Wheat Intake in Intervention study

Searching results also showed some *Food compound intake biomarkers (FCIBs)* research as defined by Q. Gao etc[18] such as phenolic compounds[21], benzoxazinoids[22] and phytoestrogen[23]. Their concentrations varied in different cereal grains. Therefore, a combination of their metabolites could potentially indicate intake of different cereals.

4 Conclusions

Currently, there's no potential biomarkers for barley intake. The biomarker (ratio of C17:0/C21:0) needs to be further validated.

5 Discussions

In order to clarify each sub-type of cereal's health beneficial effects, it is important to accurately quantify exposure amount of each sub-type. BFIs showed their strengths and potentials in studying WGs.

it is essential to discover intake biomarker for each sub-type cereal grain. Currently, most studies showed interest in WG effect biomarkers.

As discussed in [1], one of the challenges in BFIs discovery of WG is that the chemical compositions of most of WGs were not systematically

due to limited systematic research on phytochemicals

6 Appendix

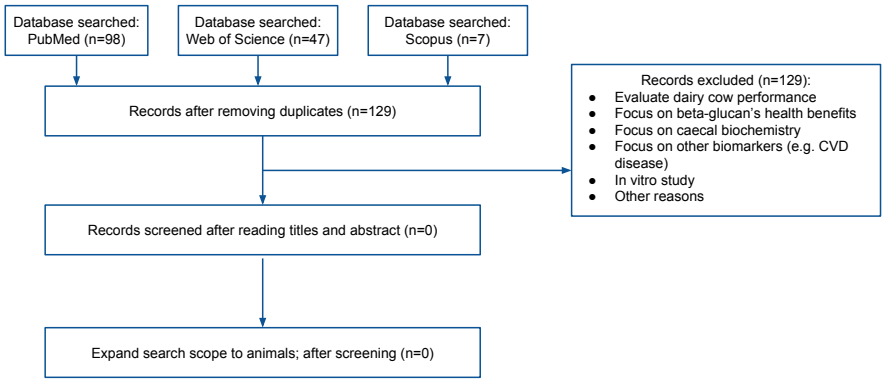

Figure 1: Flow chart of literature searching and screening for articles of barley intake biomarkers

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