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 in 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 cereal types could benefit health differently. Therefore, discovering biomarkers of each whole grain sub-type exposure could be helpful to better understand each cereal type's health beneficial effects. Hence, better dietary guidelines could be suggested to the public.

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)

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

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Some keywords were used to search in 3 database (PubMed, Web of Science, Scopus).

*Other database included HMDB, FoodDB, PhenolExplorer.

3 Results

3.1 WG barley

The literature search got 129 records after removing duplicate records from merged 3 database search results. 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[5].

A 2-month intervention study[6] incorporated 75% refined drum wheat and 25% WG barley. The fecal samples showed significant change in microbiota and metabolome after intervention[6]. However, no specific metabolite can indicate WG barley intake.

ARs and their metabolites may not indicate WG barley intake. Several observation studies[7, 8] investigated correlation between ARs metabolites and whole grain intake. Although these studies tried to cover many whole grain species, for example, one study[8] listed 7 types of regularly consumed WGs in American populations in the FFQ (Food Frequency Questionnaire)[1], barley 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 [9–11](unit: µg/g dm)

Most research results focused on barley's *effect biomarkers* as defined by Dragsted[12] and Gao[13], 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

[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

No	Candidate biomarker	Formula	Chemical group	Presence in Food	Reference
1	Hordenine	C10H15NO	alkaloid	germinating barley, beer and other plants	[14]
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

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.

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 processing methods and grain species, ARs concentration varied in WG rye and wheat. In order to distinguish wheat and rye intake, the 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[15].

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	[15]

Table 3: Potential Biomarkers of Wheat Intake in Intervention study

Food compound intake biomarker as defined by Q. Gao etc[13]. phenolic compounds[16], benzoxazinoids[17] and phytoestrogen[18].

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

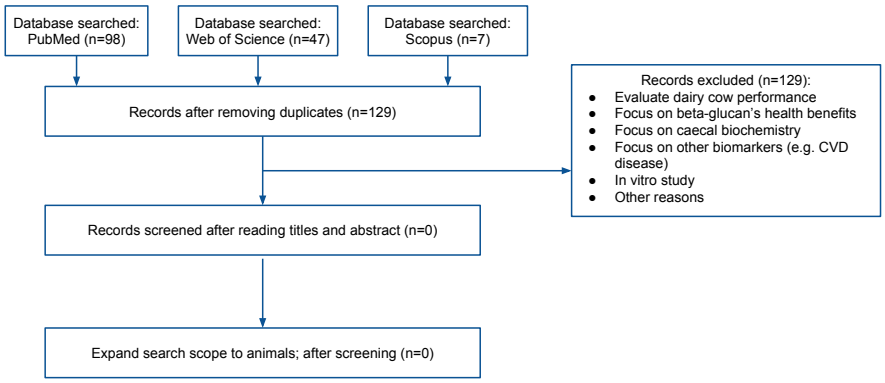

Figure 1: Flow chart of literature searching and screening for articles of barley intake biomarkers

References

1. Sang, S. Biomarkers of Whole Grain Intake. *JOURNAL OF AGRICULTURAL AND FOOD CHEMISTRY* **66,** 10347–10352. ISSN: 0021-8561 (Oct. 2018).
2. Scalbert, A. *et al.* The food metabolome: a window over dietary exposure. *The American Journal of Clinical Nutrition* **99,** 1286–1308. ISSN: 0002-9165. https://academic.oup.com/ajcn/article/99/6/1286/4577352 (June 2014).
3. Ross, A. B., Kamal-Eldin, A. & Åman, P. *Dietary Alkylresorcinols: Absorption, Bioactivities, and Possible Use as Biomarkers of Whole-grain Wheat- and Rye-rich Foods* 2004.
4. Praticò, G. *et al.* Guidelines for Biomarker of Food Intake Reviews (BFIRev): How to conduct an extensive literature search for biomarker of food intake discovery. *Genes and Nutrition* **13.** ISSN: 18653499 (2018).
5. Baik, B.-k. & Ullrich, S. E. Barley for food : Characteristics , improvement , and renewed interest. *Journal of Cereal Science* **48,** 233–242 (2008).
6. De Angelis, M. *et al.* Effect of Whole-Grain Barley on the Human Fecal Microbiota and Metabolome. eng. *Applied and environmental microbiology* **81,** 7945–7956. ISSN: 1098-5336 (Electronic) (Nov. 2015).
7. Ma, J. *et al.* Plasma Alkylresorcinols, Biomarkers of Whole-Grain Intake, Are Related to Lower BMI in Older Adults. *JOURNAL OF NUTRITION* **142,** 1859–1864. ISSN: 0022-3166 (Oct. 2012).
8. Guyman, L. A. *et al.* Urinary 3-(3,5-dihydroxyphenyl)-1-propanoic acid, an alkylresorcinol metabolite, is a potential biomarker of whole-grain intake in a US population. *JOURNAL OF NUTRITION* **138,** 1957–1962. ISSN: 0022-3166 (Oct. 2008).
9. Ross, A. B. *et al.* Alkylresorcinols in Cereals and Cereal Products. *Journal of Agricultural and Food Chemistry* **51,** 4111–4118. https://doi.org/10.1021/jf0340456 (2003).
10. Andersson, A. A. M., Åman, P., Wandel, M. & Frølich, W. Alkylresorcinols in wheat and rye flour and bread. *Journal of Food Composition and Analysis* **23,** 794–801. ISSN: 0889-1575. http://www.sciencedirect.com/science/article/pii/S0889157510001341 (2010).
11. Bordiga, M. *et al.* Alkylresorcinol content in whole grains and pearled fractions of wheat and barley. *Journal of Cereal Science* **70,** 38–46. ISSN: 0733-5210. http://www.sciencedirect.com/science/article/pii/S0733521016300790 (2016).
12. Dragsted, L. O. *et al.* Dietary and health biomarkers—time for an update. *Genes and Nutrition* **12,** 1–7. ISSN: 18653499 (2017).
13. Gao, Q. *et al.* A scheme for a flexible classification of dietary and health biomarkers. *Genes & Nutrition* **12,** 34. ISSN: 1865-3499. https://doi.org/10.1186/s12263-017-0587-x (Dec. 2017).

14. Gurdeniz, G. *et al.* Detecting Beer Intake by Unique Metabolite Patterns. eng. *Journal of proteome research* **15,** 4544–4556. ISSN: 1535-3907 (Electronic) (Dec. 2016).

15. Raninen, K. J. *et al.* Fiber content of diet affects exhaled breath volatiles in fasting and postprandial state in a pilot crossover study. *NUTRITION RESEARCH* **36,** 612–619. ISSN: 0271-5317 (June 2016).

16. Bresciani, L. *et al.* Bioavailability and metabolism of phenolic compounds from wholegrain wheat and aleurone-rich wheat bread. *MOLECULAR NUTRITION & FOOD RESEARCH* **60,** 2343–2354. ISSN: 1613-4125 (Nov. 2016).

17. Jensen, B. M. *et al.* Quantitative analysis of absorption, metabolism, and excretion of benzoxazinoids in humans after the consumption of high- and low-benzoxazinoid diets with similar contents of cereal dietary fibres: a crossover study. *EUROPEAN JOURNAL OF NUTRITION* **56,** 387–397. ISSN: 1436-6207 (Feb. 2017).

18. Nybacka, S., Forslund, H. B. & Hedelin, M. Validity of a web-based dietary questionnaire designed especially to measure the intake of phytoestrogens. *JOURNAL OF NUTRITIONAL SCIENCE* **5.** ISSN: 2048-6790 (Sept. 2016).