Author’s response to reviews

Title: Low-dose menaquinone-4 improves gamma-carboxylation of osteocalcin in young males: a non-placebo-controlled dose-response study

Authors:

Eriko Nakamura (eri.nakamura@kyowa-kirin.co.jp)
Mami Aoki (mami.aoki@kyowa-kirin.co.jp)
Fumiko Watanabe (fumiko.watanabe@kyowa-kirin.co.jp)
Ayako Kamimura (ayako.kamimura@kyowa-kirin.co.jp)

Version: 3
Date: 13 August 2014

Author’s response to reviews: see over
Dear Dr. Gabriel,

We are delighted to resubmit our manuscript, titled “Low-dose menaquinone-4 improves γ-carboxylation of osteocalcin in young males: a non-placebo-controlled dose-examination study” for publication in *Nutrition Journal* as a short report.

We greatly appreciate the editors’ and reviewers’ valuable comments and critical suggestions, which have helped us significantly improve the manuscript. As indicated in the responses in the following pages, we have taken the reviewers’ comments and suggestions into account in our revised manuscript. Also, we have corrected the grammatically mistakes in each section and modified the references according to the “instructions” of *Nutrition Journal*. Additionally, we would like to added the explanations to the text related the reference [11] (Introduction, line 51) and the time of taking capsules (Methods, line 75). The revised sentences are highlighted in red font.

We believe that the manuscript will be of considerable interest to readers of *Nutrition Journal* and look forward to hearing from you concerning your editorial decision.

Yours sincerely,

Eriko Nakamura
Healthcare Products Development Center, KYOWA HAKKO BIO CO., LTD.
2 Miyukigaoka, Tsukuba, Ibaraki, 305-0841, Japan.
Telephone: (+81) 29-856-4255; Fax: (+81) 29-856-4288
E-mail: eri.nakamura@kyowa-kirin.co.jp
Responses to Reviewer 1 (Dr. Kiyoshi Tanaka)

Minor Essential Revisions


Answer: We appreciate for your helpful comments. We have re-checked the Japanese dietary reference intakes (DRIs) 2010. The adequate intake in the DRIs is 60 µg/day in females aged 18 to 29 years. Therefore, we have not changed the text (Discussion, line 135 to 136).

2. Page 9, Line 131: The expression "less than the DRIs" should be changed to such as "less than the adequate intake (AI) in the DRIs". DRIs denotes the whole system, not a single parameter

Answer: In response to your comments, we have modified the text to: “Dietary vitamin K intake tends to be low in the British population [15] and to be less than the adequate intake in the DRIs in North America [5]” (Discussion, line 134 to 135).
Responses to Reviewer 2 (Dr. Katharina Nimptsch).

Minor essential revision

(1) Abstract: Introduction, first sentence: The term “used” is misleading here (maybe replace with “has a physiological function in …”). Conclusion is misleading: Please rephrase “a daily lower menaquinone-4 intake below 1500 μg/day improved vitamin K status”.

**Answer:** We greatly appreciate for your helpful comments about abstract. In response to your comments, we have modified the first sentence to; “Menaquinone-4 is a type of vitamin K that has a physiological function in maintaining bone quality via γ-carboxylation of osteocalcin.” (Abstract, line 13 to 14). Furthermore, we have rephrased the conclusion to; “This preliminary graded-dose study suggested that menaquinone-4 supplementation at 600 μg/day or more is likely to be important in terms of vitamin K requirements for bone health.” (Abstract, line 23 to 25).

(2) Introduction, page 4, lines 39-40: This cut-off is the result of one study, so should be described with more modesty.

**Answer:** In response to your comments, we have modified the text to; “the cut-off value of 4.5 ng/mL for ucOC has been validated [3] and is generally accepted in the selection of Japanese patients for medication for osteoporosis.” (Introduction, line 39 to 41).

(3) Quality of written English: Needs some language corrections before being published

**Answer:** We appreciate for your valuable comments about language. We have modified grammatically mistakes and our manuscript has been received a copyediting service before resubmitting.
Response to Reviewer 3 (Dr. Masao Kaneki).

Reviewer’s report:
I recommend that the manuscript be accepted.

Answer: We greatly appreciate for your consideration on our manuscript.