



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

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(21) International Application Number: PCT/CA99/00893 (22) International Filing Date: 27 September 1999 (27.09.99) (30) Priority Data: 2,265,921 8 April 1999 (08.04.99) CA 60/128,358 8 April 1999 (08.04.99) US (71)(72) Applicant and Inventor: KHAN, Airudin, S. [CA/CA]; Suite 204, 279 Wharncliffe Road North, London, Ontario N6H 2C2 (CA).		(81) Designated States: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG). Published <i>With international search report.</i>
(54) Title: COMPOSITION, CONTAINING SUBLIMED SULFUR, FOR THE TREATMENT OF LACTOSE INTOLERANCE (57) Abstract Lactose intolerance is due to lactase deficiency. Lactase is a Sulfur-containing enzyme. Sulfur, mixed with molasses, has been used as a laxative. The study included 11 patients, 7 men and 4 women, with severe lactose intolerance for over 1 year; intake of milk and milk products caused diarrhea, abdominal pain, distention, bloating, and flatulence within 15 minutes to 1 hour. After confirmation of lactose intolerance by a lactose-free diet for 1 week, the patients were placed simultaneously on a lactose-free diet and Sublimed Sulfur 200 mg, 1 capsule orally pc bid for 15 days, after which they initiated a regular diet including milk and milk products and continued Sublimed Sulfur 200 mg, 1 capsule orally pc bid for a further 30 days. Patients with diarrhea from causes other than milk and milk products were excluded from the study. The patients did not take Beta-D-galactosidase during the study. During the third week of therapy with Sublimed Sulfur, the 11 patients became symptom-free for diarrhea, abdominal pain, bloating and flatulence; and remained lactose tolerant without further treatment. One of the 11 patients relapsed after 57 weeks; lactose tolerance was restored to this patient after another course of treatment with Sublimed Sulfur; another patient relapsed after 14 weeks and did not receive further treatment. There were no side-effects to therapy with Sublimed Sulfur. A regimen of therapy with Sublimed Sulfur restores lactose tolerance in subjects with lactose intolerance without causing side effects.		

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COMPOSITION, CONTAINING SUBLIMED SULFUR, FOR THE TREATMENT OF LACTOSE INTOLERANCE

DESCRIPTION

Background Lactose intolerance, which is due to intestinal lactase deficiency, is worldwide in distribution, affecting 50 percent of Orientals, 90 percent of Africans and 30 percent of Caucasians. Lactose intolerance, which varies in severity from mild to very severe, increases in incidence with increasing age. Lactase is a Sulfur-containing enzyme. Sulfur, mixed with molasses, has been used as a laxative.

Methods A 45 year old man with a confirmed plasma homocysteine level of 77 $\mu\text{mol/L}$ had lactose intolerance for 3 years; butter, cheese, cream, milk, ice cream, yogurt and foods containing milk products precipitated abdominal cramps, abdominal distension, bloating and flatulence lasting 60 to 90 minutes, followed by diarrhea within 1 hour. He occasionally obtained partial relief and sometimes complete relief from the abdominal symptoms by taking 5 tablets of extra strength Beta-D-galactosidase everyday. With his consent, he was conscripted as the initial subject of a study investigating the effect of Sublimed Sulfur on plasma homocysteine levels. His plasma homocysteine decreased by 89.4 percent as a result of therapy with Sublimed Sulfur 300 mg orally bid pc for 45 days. In addition, lactose tolerance was restored to this man by Sublimed Sulfur therapy and he no longer suffered from abdominal cramps, abdominal distension, bloating, flatulence and diarrhea and he remained symptom-free after discontinuation of Sublimed Sulfur. He subsequently developed lactose intolerance 57 weeks after discontinuation of the initial course of Sublimed Sulfur and was placed on another course of Sublimed Sulfur 200 mg orally bid pc for 6 weeks. Lactose tolerance was again restored to him after completing 2 weeks of the second course of treatment with Sublimed Sulfur.

A more extensive study was undertaken. 11 patients, 4 females and 7 males were recruited because of lactose intolerance for over 1 year and symptoms of diarrhea, abdominal pain, distension, bloating and flatulence within 15 minutes to 2 hours after intake of milk and milk products. Following confirmation of lactose intolerance by a

lactose free diet for 1 week, subjects were placed simultaneously on a lactose free diet and Sublimed Sulfur 200 mg., 1 capsule orally pc bid for 15 days, after which they initiated unrestricted oral intake of milk and milk products and continued Sublimed Sulfur 200 mg, 1 capsule orally pc bid for a further 30 days. Serum vitamin B12 and erythrocyte folic acid levels were obtained within the 24 hours immediately preceding the first daily dose of Sublimed Sulfur. A record was kept of the presence or absence of symptoms of lactose intolerance. Exclusion criteria for the study included diarrhea from causes other than milk and milk products. Beta-D-galactosidase was not taken by the patients during the course of the study.

Results Lactose tolerance was restored to the 11 patients with lactose intolerance during the third week of therapy with Sublimed Sulfur; on a regular diet, 10 of the 11 patients became symptom-free for diarrhea, abdominal pain, distension, bloating and flatulence, whereas flatulence persisted in a vitamin B12 deficient patient despite supplemental vitamin B12. He remained asymptomatic for diarrhea and abdominal pain, distension and bloating for 14 weeks after discontinuation of Sublimed Sulfur. (Table 1)

Discussion This study provides evidence that treatment with elemental Sulfur restores lactose tolerance in patients with lactose intolerance. The restoration of lactose tolerance is evidence that intestinal mucosal lactase production is restored, either by alteration of the metabolism of the Sulfur-containing essential amino acids, or by stimulation of the production of a Sulfur-containing precursor of lactase which is a Sulfur-containing enzyme. Further investigations are indicated in order to determine the biochemical mechanisms by which Sublimed Sulfur restores lactase production. The persistence of lactose tolerance for up to 57 weeks after discontinuation of Sublimed Sulfur therapy suggests that Sublimed Sulfur is retained and utilized or re-utilized for the continuing synthesis of lactase.

Conclusions A regimen of treatment with Sublimed Sulfur restores lactose tolerance in patients with lactose intolerance. The lactose tolerance persists during treatment with Sublimed Sulfur and after discontinuation of Sublimed Sulfur therapy. Lactose tolerance is restored by Sublimed Sulfur therapy to patients who develop lactose intolerance after discontinuation of Sublimed Sulfur.

Table 1. Effects of Sublimed Sulfur on Lactose Intolerance

Subject	Age /Sex	Symptoms Before Treatment		Date Sublimed Sulfur Started	Symptoms During Treatment		After Discontinuation of Sublimed Sulfur
		Regular Diet	Lactose Free Diet for 1 week		Lactose Free Diet and Sublimed Sulfur for 15 Days	Regular Diet and Sublimed Sulfur for 30 Days	Number of Symptom Free Weeks ² on Regular Diet
1	54/F	+	-	January 20/99	-	-	33
2	40/M	+	FI	January 27/99	FI	FI	14 R
3	69/M	+	-	April 16/99	-	-	21
4	46/F	+	-	April 19/99	-	-	20
5	28/M	+	-	May 28/99	-	-	15
6	66/F	+	-	June 26/99	-	-	11
7	43/M	+	-	June 29/99	-	-	10
8	26/F	+	-	July 06/99	-	-	9
9	30/M	+	-	September 03/99	-	- s	s
10	72/M	+	-	September 07/99	-	- s	s
11	40/M	+	-	September 08/99	-	- s	s

+ Diarrhea, Abdominal Pain, Distension, Bloating and Flatulence

- Diarrhea, Abdominal Pain, Distension, Bloating and Flatulence no longer present

FI Persistence of Flatulence

R Symptoms Recurred 14 weeks after discontinuation of Sublimed Sulfur

2 At the time of writing

s Still on treatment at the time of writing

Claims

1. A regimen of treatment with Sublimed Sulfur restores lactose tolerance in patients with lactose intolerance.
2. The lactose tolerance as defined in claim 1 persists while treatment with Sublimed Sulfur is continued.
3. The lactose tolerance as defined in claim 1 and claim 2 persists after Sublimed Sulfur is discontinued.
4. A regimen of treatment with Sublimed Sulfur as defined in claim 1, claim 2 and claim 3 restores lactose tolerance in patients who develop lactose intolerance after Sublimed Sulfur is discontinued.

INTERNATIONAL SEARCH REPORT

International Application No

PCT/CA 99/00893

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61K33/04

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	EP 0 581 972 A (VERDE GIANCARLO U) 9 February 1994 (1994-02-09) claims ---	1-4
A	EP 0 615 757 A (GRIMBERG GEORGES SERGE) 21 September 1994 (1994-09-21) page 2 ---	1-4
A	FR 2 228 470 A (DEGEMONT MARGUERITE) 6 December 1974 (1974-12-06) claims ---	1-4
A	US 4 976 970 A (LANDY WADY N) 11 December 1990 (1990-12-11) claims -----	1-4



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

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Date of the actual completion of the international search

21 March 2000

Date of mailing of the international search report

29/03/2000

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Leherte, C

INTERNATIONAL SEARCH REPORT

International application No.

PCT/CA 99/00893

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
Remark: Although claim(s) 1-4
is(are) directed to a method of treatment of the human/animal
body, the search has been carried out and based on the alleged
effects of the compound/composition.
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such
an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all
searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment
of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report
covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is
restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/CA 99/00893

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