



Original

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## Nutritional analysis of diet at base camp of a seven thousand-metre mountain in the Himalayas

M. Mariscal-Arcas<sup>a</sup>, C. Carvajal<sup>a</sup>, C. Monteagudo<sup>a</sup>, J. Lahtinen<sup>d</sup>, M. C. Fernández de Alba<sup>b</sup>, B. Feriche<sup>c</sup> and F. Olea-Serrano<sup>a</sup>

<sup>a</sup>Nutrition and Food Science Department. University of Granada. Spain.

<sup>b</sup>Andalusian Centre of Sport Medicine (CAMD). Junta de Andalucía. Spain.

<sup>c</sup>Physical Education and Sport Department. University of Granada. Spain.

<sup>d</sup>Altitude Training Centre (CAR) of Sierra-Neveda. Consejo Superior de Deportes (CSD). Spain.

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### ABSTRACT

**Objective.** To evaluate the diet of a group of high-mountain climbers at 4,500 metres.

**Methods.** A descriptive cross-sectional study was performed on the diet of a group of high-mountain climbers at their base camp (4,500 m).

**Results.** The mean intake was 11.85 MJ/day (2,833 kcal/day), which provided an inadequate supply of energy and micronutrients to replenish deposits. Their mean carbohydrate intake (39.5%) was excessively low, since carbohydrate-rich diet favours acclimatization and the capacity for recovery. Their daily intake of 1.5-2.5 g/protein/kg of bodyweight was very similar to recommendations (1.5-2.0 g/kg/day).

**Conclusions.** The climbers underwent a drastic change from their habitual Mediterranean diet, rich in monounsaturated fats (largely olive oil), to a diet rich in polyunsaturated fats (largely soy oil). The Sherpa-prepared diet on this expedition was not balanced. It was rich in saturated polyunsaturated fats and relatively poor in proteins and especially carbohydrates, similar to the traditional diet of climbers. Dietary strategies need to be developed to increase the intake of nutrients that favours the physical recovery of climbers and their altitude-acclimatization and to avoid micronutrient deficiencies.

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### RESUMEN

#### Análisis nutricional de la dieta en un campamento base a 7.000 metros en una montaña del Himalaya

**Objetivo.** Evaluación de la dieta de un grupo de escaladores de alta montaña a 4.500 metros.

**Método.** Estudio descriptivo de corte transversal realizado sobre la dieta de un grupo de escaladores de alta montaña en su campamento base (4.500 m).

**Resultados.** La ingesta media fue de 11,85 MJ/día (2.833 kcal/día), que proporcionan un suministro inadecuado de energía y micronutrientes para reponer los depósitos. El consumo promedio de los hidratos de carbono (39,5%) era excesivamente bajo, ya que la aclimatación y la capacidad de recuperación se favorece con una dieta rica en carbohidratos. La ingesta diaria de 1,5-2,5 g/proteína/kg de peso corporal fue muy similar a las recomendaciones (1,5-2,0 g/kg/día).

**Conclusiones.** Los escaladores sufrieron un cambio drástico de su dieta mediterránea habitual, rica en grasas monoinsaturadas (aceite de oliva en gran medida), al pasar a una dieta rica en grasas poliinsaturadas (principalmente aceite de soja). La dieta preparada por los serpas, en esta expedición, no era equilibrada. Era una dieta rica sobre todo en grasas saturadas y poliinsaturadas, relativamente pobre en proteínas y carbohidratos, similar a la dieta tradicional de los escaladores. Se deben desarrollar estrategias en la dieta para aumentar la ingesta de nutrientes que favorezcan la recuperación física de los escaladores y su aclimatación a la altura y así evitar carencias de micronutrientes.

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### Correspondence:

F. Olea-Serrano.

Nutrition and Food Science Department.

University of Granada.

Campus de Cartuja s/n

18071 Granada. Spain.

E-mail: folea@ugr.es

## Introduction

Nutrition plays an important role in the achievement of optimal performance in sports and is especially critical in resistance sports. The resistance sport of alpinism combines high physical exercise with hypoxia-induced anorexia, especially at altitudes above 6,000 metres. Studies have shown that the organism can oxidize fats and carbohydrates in a normal manner up to 5,000 metres, therefore any weight loss below this altitude can be attributed to inadequate calorie intake<sup>1-3</sup>. Weight loss above 5,000 metres appears inevitable due to the loss of appetite and nausea produced by altitude sickness and the metabolic changes required to obtain energy.

It has generally been accepted that the human diet should contain 55-65% carbohydrates, 12-20% proteins and 20-30% fats<sup>4</sup>, although the WHO recently increased the recommended proportion of carbohydrates to 75%<sup>5</sup>. However, some authors have supported increasing the protein intake at the expense of fats at high altitudes, with each component comprising 15-20% of the diet. They propose a daily intake of at least 7 g of carbohydrates per kg of weight (3.2 g per pound) plus 1.5-2.0 g of protein, with remaining calories consumed as fats<sup>6</sup>. Special caution should be taken with traditional fat-rich diets, which can lead to chronic muscle fatigue; they provide an inadequate amount of readily available carbohydrates, and diets rich in fatty acids require more oxygen during metabolism, slowing acclimatization. In a hypobaric chamber study<sup>7</sup>, in which altitude hypoxia was simulated by the gradual decompression of the chamber, subjects consumed *ad libitum* from a range of appetizing dishes but lost weight in proportion to the simulated altitude *versus* controls offered the same food under normal pressure conditions. Therefore, hypobaric hypoxia appears to be sufficient to produce weight loss, probably due to anorexia and poor intestinal absorption. These effects are increased in real expeditions<sup>8,9</sup>.

Oxygen saturation values of around 70% are essential for good absorption in the small intestine and avoidance of weight loss<sup>10-11</sup>. Roberts et al<sup>12</sup> suggested that acclimatized individuals may have lower fat metabolism activity at high altitudes, influencing carbohydrate availability. On the other hand, McClelland et al<sup>13</sup> concluded that the relative carbohydrate contribution does not change after altitude acclimatization and that the metabolic utilization of fuel is mainly influenced by the relative intensity of exercise, as at sea level.

There is little evidence that chronic or acute exposure to altitude increases the demand for any specific micronutrient, although there have been reports that iron and vitamin E supplements may be beneficial<sup>14</sup>. Studies of the effects of cold, energy expenditure, ultraviolet ray exposure and atmospheric composition indicate that supplementation with certain vitamins has a highly desirable antioxidant function in the high mountains<sup>15-18</sup>. At high altitudes, the prolonged consumption of vitamins with antioxidant properties can prevent the slowing of blood flow and the reduction in physical function associated with free-radical induced damage<sup>19,20</sup>. Dietary treatments that preserve or enhance the fluidity or deformability of the red blood cell membrane improve the transfer of oxygen to tissues, and action to improve oxygen delivery to tissues under hypoxia conditions is generally advantageous for the functioning of the organism. Exposure to hypoxia and peroxidation of unsaturated fatty acids of the red blood cell membrane reduce its deformability and its capacity to adapt to capillaries. Improved membrane fluidity (increased deformation capacity) can be achieved by two dietary mechanisms, for instance, diet supplementation with polyunsaturated fatty acids

or antioxidants (for instance, vitamin E), in order to protect polyunsaturated fatty acids in membranes from peroxidation by free radicals.

Iron supplements can also be beneficial in this situation. According to observations of the response of erythropoiesis and haemoglobin synthesis at high altitudes, a normal iron intake appears adequate for males, whereas women may benefit from iron supplementation. The intake of oral iron supplements (ferrous sulphate, 200-300 mg/day) has been proposed during 2-3 weeks before a climb and during 2-4 weeks while at altitude, with the caveat that an increase in free radicals may be produced<sup>21-23</sup>.

In November and December 2002, seven climbers from Andalusia (Southern Spain) attempted the ascent of Jannu ("sleeping giant" in Nepalese), a Himalayan mountain of 7,710 meters in the Kangchenjunga region of Nepal.

The objective of the present study was to evaluate the diet of a group of high-mountain climbers at 4,500 metres, analyzing the types and amounts of nutrients.

## Methods

### Subjects

A study was undertaken of the diet followed by seven male climbers on the "Andalusia K2 2003" expedition; they were aged from 27 to 42 years and all had considerable mountaineering experience. Before acceptance as expedition member, each was informed both verbally and in writing of the full extent of the proposed research, and written informed consent was then obtained from each subject. All were in excellent physical condition prior to departure. Table 1 lists the responsibilities of expedition members and their anthropometrical parameters, calculated according to FAO/WHO<sup>24</sup>.

### Procedure

The expedition comprised two phases: firstly ascent of Jannu in October, November, and December 2002; and secondly ascent of K2 (at 8,611 meters, the second highest mountain in the world) in June, July, and August 2003. The expedition was organized by the Andalusian Mountaineering Federation and subsidized by the Department of Tourism and Sports of the Andalusian Regional Government. The investigation was approved by the ethics committee of the University of Granada and all subject data were coded to maintain confidentiality.

### Food and supplements

A register was pre-prepared for recording all data related to nutrition throughout the expedition. We recorded and analysed all of the food consumed at base camp during a 17-day period. Food items were brought from Katmandu and prepared by two Sherpa cooks.

Four daily meals were prepared: breakfast, mid-morning snack, lunch, and evening meal. Varied menus were provided during the 17-day study period, prepared from both fresh and preserved foods. The amounts were calculated from the weight of the food items, measured by the climber responsible for food. They were weighed by means of a kitchen scale of 2 kg capacity with 20 g increments (Hanson UK Ltd.

**Table 1**  
Responsibilities and characteristics of expedition members

	Leader	Sub-Leader	Technical material	Physician	Audiovisual materials	Communications	Food	Mean
Age (years)	37.00	42.00	30.00	38.00	36.00	39.00	27.00	35.57
Initial weight (kg)	65.20	68.30	71.30	72.00	66.00	80.40	71.10	70.61
Final weight (kg)	62.00	65.10	67.30	70.30	63.20	75.40	66.20	67.07
Weight difference (kg)	3.20	3.20	4.00	1.70	2.80	5.00	4.90	3.54
Height (m)	1.71	1.72	1.78	1.80	1.72	1.80	1.74	1.75
Initial BMI (kg/m <sup>2</sup> )	22.23	22.98	22.41	22.22	22.31	20.83	23.45	22.35
BMR (MJ)*	6.77	6.92	7.10	7.11	6.82	7.49	7.37	7.08

\*Calculated according to FAO/WHO, 2001 (18-30 years old, 0.063 kg + 2.896; 30-60 years old, 0.048 kg + 3.653). Mean weight loss = 3.57 kg. BMR: basal metabolic rate.

**Table 2**  
Description of the foods consumed at base

Vegetables	Consumption (g and g/day)	Frequency during 17 days	Protein foods	Consumption (g and g/day)	Frequency during 17 days	Fruit	Consumption (g and g/day)	Frequency during 17 days
Carrot purée	300 (75)	4	Egg	1,200 (150)	8	Preserved compote	1,440 (180)	8
Carrot	847 (60)	14	Lean yak steak	1,500 (100)	15	Peach in syrup	1,080 (180)	6
Cabbage	375 (75)	5	Canned sardines	125	1	Preserved mango	600 (200)	3
Boiled potatoes	800 (115)	7	Frankfurt sausage	325 (65)	5	Sugar	140 (10)	14
Preserved sweet corn	50	1	Tuna in pastry	200	1	Honey	20	1
Endives	180 (90)	2	Breaded chicken	120	1	Homemade chocolate cake	150	1
Cauliflower	75	1	Potato omelet	1,350 (150)	9	Cinnamon sponge cake	150	1
Cauliflower cheese	300 (75)	4	Powdered whole cow's milk	1,800 (165)	11	Custard	250 (125)	2
Mushrooms	470 (94)	5	Yak cheese	180 (20)	9	Jam	25	1
Peas	240 (80)	3	Carbohydrate foods			Wheat bread	100	1
Onion, garlic	150 (30)	5	White rice	350 (87.5)	4	Other food		
Vegetable soup	250	1	Corn flour	165 (55)	3	Mayonnaise	40	1
Green beans	120 (40)	3	Cornflakes	180 (30)	6	Packet soups	200 (25)	8
Lettuce	200 (50)	4	Chapatti with egg	575 (115)	5	Pizza	550 (275)	2
Corn	1,400 (100)	14	Popcorn	500 (100)	5	Tea	4,250 (250)	17
Chickpeas	160 (80)	2	Pasta	480 (80)	6	Spices (pepper, mustard, etc.)	Ad libitum	
Tomato sauce	660 (55)	12	Pasta with vegetables	640 (80)	8			
			Chapattis	100	1	<b>Fats</b>		
			Potato chips	100	1	Butter	20	1
			Spaghetti in white sauce	80	1	Soy oil	Ad libitum	17

ref. 205 H, 700320363 Rev. 6.11). The same climber maintained the register, in which all foods purchased were noted and the food consumed on each day was recorded. The diet was analyzed by using the Dietsource software package<sup>25</sup>. When necessary, information on the composition of local foods (for instance, yak meat) was added to the database of this program, derived from the Food Composition Table for use in East Asia<sup>26</sup>. The energy intake (EI) was estimated from the daily menus. All mountaineers ate exactly the same meals and always ate all of the food offered, therefore the daily EI can be assumed to be identical for all study subjects. The estimated-EI value was related to the total energy expenditure (TEE) according to equations proposed by FAO/WHO<sup>24</sup> ( $TEE = 662 - 9.53 \times \text{age (years)} + PA \times 15.91 \times \text{weight (kg)} + 539.6 \times \text{height (m)}$ ), taking account of the basal metabolic rate (BMR) and physical activity level (PAL) of the group<sup>27</sup>. TEE values were calculated considering active PAL values (1.70-1.99) or, on climbing days, vigorous PAL values (2.00-2.40) PAL values.

### Statistical analysis

Mean, minimum and maximum levels of nutrients in the menus were calculated, and the Student's t-test was used to compare nutritional data gathered during the 17 days of the expedition (estimated-EI) with nutrient intake recommendations (2005 Dietary Reference Intakes [DRI] data) for this population<sup>28</sup>. The normal distribution of nutrient values was checked and confirmed by using Kolmogorov-Smirnov and Shapiro-Wilke tests<sup>29,30</sup>.  $P < 0.05$  was considered statistically significant. SPSS version 15.0 software was used for all data analyses.

### Results

Table 2 lists food groups in the diet, amounts per person and frequency of their consumption. Tables 3 and 4 show results of the nutritional analysis of the meals consumed at the base camp during the 17-day

**Table 3**

Nutrients and energy provided by the diet and mean distribution of fats in studied diet

Nutrients/day	Minimum	Maximum	Mean	SD	% energy
Proteins (g)	22.30	167.10	110.70	46.20	15.50
Fats (g)	60.90	206.10	142.10	47.60	45.50
Carbohydrates (g)	94.10	399.90	277.60	84.80	39.50
Fiber (g)	3.90	20.00	12.60	4.80	
Energy (MJ)	4.83	16.70	11.85	3.77	100.00
Saturated fats (g)	8.90	73.10	38.00	20.30	33.60*
Monosaturated fat (g)	19.70	37.40	25.50	7.50	27.60*
Polysaturated fat (g)	20.20	77.70	49.40	5.20	43.70*
Cholesterol (mg)	104.00	2,164.00	1,051.70	618.90	

\*% energy from 45.5 fats energy.

SD: standard deviation.

study and the comparison (Student's t-test for one sample) with DRI values. Minimal estimated-EI (calculated from mean portions consumed by the group) and hence minimal estimated-EI/BMR ratios were observed on days 1 and 11 of the base camp stay. The mean estimated-EI/BMR (SD) of the group was 1.67 (0.53), ranging from 0.64 to 2.47. Table 5 shows the comparison between the TEE values calculated for each climber (according to weight, age and physical activity) and their estimated-EI values (see table 5 footnotes). When active PAL values were considered, no differences between mean estimated-EI and TEE values were found, but when vigorous PAL values were assumed, significant differences ( $P < 0.05$ ) were found for five of the climbers.

Climbers were weighed at the start and end of the entire 2-month expedition, finding weight losses ranging from 2 to 5 kg (table 1).

## Discussion

On a high-mountain climb, 15.90–25.10 MJ (3,800–6,000 kcal) are expended daily according to the type of physical activity involved<sup>11</sup>. It is evidently important to consume the amount of calories required by the organism. Climbers lose at least 3% of their body weight after eight days at 4,300 meters and 15% after three months at 5,300–8,000 meters<sup>31</sup>. This loss can produce a reduction in mental and physical functioning. Some studies have suggested that the intake of carbohydrates at altitude

improves blood oxygenation and provides a more efficient energy source compared with fats or protein<sup>2</sup>. The macronutrient and energy levels observed in the present climbers differed widely from the usual recommendations for climbs above 6,000 meters. Nevertheless, no significant differences were found between the mean estimated-EI values estimated from the diet (11.85 MJ/day [2,832.5 kcal/day]) and the TEE values calculated for each climber according to 2001 FAO/WHO recommendations<sup>24</sup> for adults with moderate activity. When the TEE was calculated for adults engaged in vigorous activity (PAL = 2.00–2.40), however, a significant difference with the estimated-EI value was found for five climbers. It should be borne in mind that this level of activity cannot be maintained during long time periods.

Among the 17 acclimatization days studied, estimated-EI/BMR values of  $> 2.00$  were recorded on the only 7 days when they were climbing, an intake of at least 8.37 MJ/day (2,000 kcal/day) is recommended during long-duration activities to avoid iron or calcium deficits, depletion of glycogen deposits and dehydration<sup>31</sup>. Since these climbers were at 4,500 m and the aim of their base camp stay was to replenish energy deposits, their mean intake of 11.85 MJ/day (2,833 kcal/day) provided an inadequate supply of energy and micronutrients. These observations are similar to those reported by most studies, either in hypobaric chamber or *in situ*<sup>3</sup>.

The production of energy per litre of oxygen is higher when carbohydrates are the energy source, regardless of the oxygen pressure of inhaled air. Carbohydrates are also a more efficient energy source for working under conditions of reduced oxygen pressure<sup>32</sup>. The 39.5% carbohydrate intake of the present study group was very low, since around 55–65% is usually recommended to avoid muscle exhaustion from excessive depletion of glycogen reserves and to maintain adequate glycaemia against excessive protein catabolism. In short, a carbohydrate-rich diet favours acclimatization and the capacity for recovery<sup>4,31</sup>.

The climbers had a daily intake of 1.5–2.5 g of proteins per kg of bodyweight, very similar to the recommendations of most authors consulted (1.5–2.0 g/kg/day)<sup>33,34</sup> and representing 12–15% of the total energy consumed<sup>35</sup>. Nevertheless, some authors have proposed a higher intake of 2.5–3 g/kg/day<sup>36</sup>. An adequate intake of proteins and glucose liquids is essential to prevent excessive weight loss under conditions of very high catabolism. Furthermore, prolonged exercise has a similar immunosuppressive effect to that of diets deficient in proteins and specific micronutrients<sup>37</sup>. Although no amino acid supplements were

**Table 4**

Mean (total/daily) intake of micronutrients during the 17 days at base camp

Nutrients intake/day	Minimum	Maximum	Mean (SD)	DRI	T Test	P
Phosphorus (mg/day)	474.6	3,027.1	1,949.2 (884.8)	700	5.647	0.0001
Magnesium (mg/day)	163.5	485.3	342.0 (108.2)	420	-2.881	0.011
Calcium (mg/day)	142.1	2,774.5	1,487.4 (1,019.0)	1,000	1.913	0.075
Iron (mg/day)	5.2	29.1	17.1 (6.3)	8	5.767	0.0001
Zinc (mg/day)	4.5	25.1	15.5 (7.4)	11	2.441	0.028
Iodine (ug/day)	7.0	101.7	47.3 (25.1)	150	-16.303	0.000
Selenium (ug/day)	6.5	78.8	38.5 (23.4)	55	-2.811	0.013
Ascorbic acid (mg/day)	18.3	277.1	89.5 (73.8)	90	-0.025	0.980
Thiamin (mg/day)	0.5	2.4	1.5 (0.6)	1.2	2.540	0.023
Riboflavin (mg/day)	0.5	6.8	3.0 (1.9)	1.3	3.648	0.002
Nicotinic acid (mg/day)	3.6	32.1	19.9 (8.7)	16	1.815	0.090
Pyridoxine (mg/day)	0.6	4.7	2.7 (1.6)	1.3	3.678	0.002
Folic acid (ug/day)	77.4	302.3	168.4 (66.8)	400	-13.852	0.0001
Cyanocobalamin (ug/day)	1.1	39.9	8.1 (8.9)	02.4	2.542	0.023
Vitamine E (mg/day)	12.8	24.5	18.8 (4.3)	15	3.55	0.003

DRI: Dietary Reference Intakes, 2005.

SD: standard deviation.

**Table 5**  
Comparison of means of EI (MJ/day) vs. TEE (MJ/day)

Climber number	TEE (active) (MJ/d)	T Test	P	TEE (vigorous) (MJ/d)	T Test	P
1	11.53	0.342	0.737	13.41	-1.653	0.119
2	11.61	0.259	0.799	13.54	-1.791	0.094
3	12.50	-0.692	0.499	14.52	-2.823	0.013
4	12.33	-0.502	0.623	14.36	-2.661	0.018
5	11.68	0.181	0.858	13.58	-1.836	0.086
6	12.95	-1.165	0.262	15.11	-3.453	0.004
7	12.51	-0.699	0.495	14.50	-2.808	0.013

Equation used in the calculation:  $TEE = 662 - 9.53 \times \text{age (years)} + PA \times 15.91 \times \text{weight (kg)} + 539.6 \times \text{height (m)}$ . PA = 1.25 if PAL is considered to be 1.70-1.99 (active); PA = 1.48 if PAL is considered to be 2-2.4 (vigorous).

PA: physical activity; TEE: total energy expenditure.

used in this expedition, some authors have proposed that valine, leucine and isoleucine supplementation prevents loss of muscle mass during acute hypobaric hypoxia<sup>38</sup>. In fact, the intake of these amino acids by the present climbers was similar to levels recommended for the general population. Supplementation with probiotics and glutamine appears to play a major role in immunofunction<sup>39</sup>. With regard to the origin of the protein, some studies have indicated that vegetable proteins produce a small reduction in free fatty acids<sup>40</sup>, which could be beneficial in diets that are very rich in fats.

In contrast to their carbohydrate content, the fat levels of the present diet were excessively elevated (45%). According to the American Dietetic Association and the American College of Sports Medicine<sup>31</sup>, fats should constitute at least 15% but not more than 20-25% of a diet. As mentioned above, fats are not the most efficient energy source under hypoxia conditions. The overconsumption of fats is a frequent observation, both among the general population and in different sports settings, for instance, swimming<sup>41</sup>.

Diets that are very rich in polyunsaturated fatty acids, especially linoleic acid, appear to reduce the absorption and utilization of iron, zinc and magnesium, reducing sports performance<sup>42</sup>. Nevertheless, some authors concluded that the role of linoleic acid remains unclear<sup>39</sup>. It should be taken into account that the present climbers underwent a drastic change in their diet. They all live in a Mediterranean region where fat consumption is largely in the form of olive oil, rich in monounsaturated fats (oleic acid), whereas the fats they consumed during the expedition were usually in the form of soy oil, rich in linoleic acid. Soy oil contains 45-60% linoleic acid, whereas olive oil contains 61-82% oleic acid, which presents greater resistance to auto-oxidation processes and the formation of free radicals<sup>43,44</sup>. If the climbers had used olive oil instead of soy oil, their diet would have contained a much higher proportion of monounsaturated versus polyunsaturated fats.

The well-documented importance of iron, calcium, magnesium and vitamins D and C is even greater in situations of high oxidative stress, such as those produced in high mountains and by adaptation to high altitudes<sup>45,46</sup>. The increased excretion of iron, copper and manganese in intense and prolonged exercise was reported to produce a negative mineral balance<sup>42,47</sup>, although Fogelholm<sup>39</sup> claimed neither the mineral nor vitamin balance is usually a problem for athletes, with the exception of iron and calcium in females. The supply of iron appears to have been adequate in the present study group (mean intake of 17.1 mg/day). Several authors have recommended that iron supplements may be taken up to two to three weeks before an expedition, maximizing iron levels, but once in the mountain they should only be supplied by the daily food intake,

thereby avoiding the release of free radicals produced by iron supplements in hypoxia situations<sup>48,49</sup>. Excessive micronutrient supplementation (mainly vitamin C, B-group vitamins, and iron) during climbs has been contraindicated, since it does not improve sports performance and may have undesirable effects<sup>50</sup>. Nevertheless, vitamin C and general vitamin supplementation appears to be appropriate after exercise<sup>51,52</sup>.

The diet under study showed some interesting qualitative differences with the usual traditional Mediterranean diet<sup>53</sup> of the climbers. It included novel foods such as yak products (meat, butter and cheese) and soy oil instead of olive oil, as mentioned above, and there was an absence or relative scarcity of fish, fruit, and vegetables (table 2).

The nutrient composition of the diet of these mountain climbers was not ideal. It was rich in saturated fats of animal origin and polyunsaturated fats from soy oil and was relatively poor in proteins and especially in carbohydrates, similar to the traditional diets of climbers. This type of nutrition does not favour acclimatization, because metabolism of the excessive fats requires greater supplies of oxygen at the expense of other tissues. An inadequate carbohydrate intake compromises effective muscle and liver recovery, produces a hyperglycaemia that increases protein catabolism, and accelerates weight loss<sup>54</sup>. The diet had a very low content of antioxidant vitamins, reducing the climbers' defences against free radicals and increasing the risk of damage to cell membranes. In conclusion, the diet of these climbers was not appropriate under these conditions. The lessons drawn from this study will serve to improve the nutritional intake of this team of alpinists during future expeditions.

### Conflict of interest statement

The authors declare that there are no conflicts of interest.

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