Dietary fatty acid metabolism: New insights into the similarities of lipid metabolism in humans and hamsters

Alaitz Berriozabalgoitia, Juan Carlos Ruiz de Gordoa, Gustavo Amores, Mailo Virto[*]

Lactiker Research Group, Department of Biochemistry and Molecular Biology, University of the Basque Country UPV/EHU, Paseo de la Universidad 7, 01006 Vitoria-Gasteiz, Spain

ABSTRACT

Hamsters have been long accepted as animal models to study the lipid metabolism in humans. However, very few scientific works described in detail the fatty acid (FA) composition of plasma and erythrocytes in hamsters in relation to their dietary intake, and none work was found comparing them with that described in humans. Therefore, a study was carried out to compare the effect of ingesting olive oil or dairy fat, as part of an equilibrated diet in healthy subjects, on plasma and erythrocytes FA composition. More than 40 FA were detected in samples of both species. It was demonstrated that plasma total FA (TFA) concentration and FA profiles are similar in humans and hamsters. In both species linoleic, oleic and palmitic acids are the main FA and accounted for the 70% of TFA. Differences found between species can be explained by differences in the dietary intake and differences in the proportion of triglycerides, cholesteryl esters and phospholipid fractions in plasma of both species. Changes in dietary FA intake causes similar changes in FA concentration in the plasma of both species and can be explained by the same metabolic processes. The erythrocyte FA profile differs more between the two species. Moreover, unlike humans, the FA profile of hamster erythrocytes is more sensitive to changes in dietary FA than that of plasma.

1. Introduction

The major proportion of plasma fatty acids (FA) is esterified in various lipid classes (triglycerides, TG; phospholipids, PL; cholesteryl esters, CE), which are components of lipoproteins, whereas small amounts are not esterified (NEFA) and are bound to albumin. Nevertheless, FA composition of different blood lipid fractions is interrelated (Hodson, Skeaff, & Fielding, 2008). Therefore, plasma total FA (TFA) pool represents a mixture of all lipid fractions that contain FA and also reflects the FA profile of tissues (McCloy, Ryan, Pencharz, Ross, & Cunnane, 2004).

The FA composition of plasma and tissues are the result of various processes, e.g. dietary intake, intestinal absorption, metabolism and storage and exchanges among compartments.

When the dietary fat is digested, FA are incorporated into chylomicrons in form of TG in the enterocyte and enter the systemic circulation. Afterwards, they are incorporated into endogenous lipids or enter metabolic pathways, which are specific for each FA (Hodson, McQuaid, Karpe, Frayn, & Fielding, 2008). Thus, the relationship between ingested FA and their presence in plasma lipid fractions is variable and has been extensively studied. In the review of Hodson et al. (2008) the authors conclude that, in general, positive correlations have found for polyunsaturated FA (PUFA) in either, total plasma and plasma fractions. However, for saturated FA (SFA) and monounsaturated FA (MUFA) the results are more variable and depend on the FA. For example, the correlation found between the intake of myristic acid (14:0), 14:1, 15:0 and 17:1 and the FA composition of blood lipids is, in general, strong. However, for other SFA and MUFA, the reported correlations are more variable and, generally, weaker (Hodson et al., 2008).

On the other hand, it has been demonstrated that the FA composition

of erythrocytes, which reflects mainly the composition of their membrane PL, is sensible to changes in FA composition of the diet. For example, Fuhrman et al. (2006) showed that erythrocytes membrane FA content is a valid biomarker of dietary levels of linoleic acid (18:2n-6, LA), oleic acid (*cis*9-18:1, OA) and PUFA. Berriozabalgoitia et al. (2021) found a significant correlation between dairy fat ingestion and the concentration of FA as myristic acid, 17:0 or vaccenic acid (*trans*11-18:1, VA) in erythrocytes.

In the scientific literature, special attention has been paid to the effect of dairy fat ingestion on plasma lipids because of its relatively high content of saturated fat and the conflicting health effects described in the literature (Thorning et al., 2017). However, dairy fat has been also extensively studied because of its unique FA composition. More than 400 different FA have been identified in bovine dairy fat. Some of them are synthesized de novo by rumen bacteria. For example, *trans*-FA, primarily VA and rumenic acid (*cis*9,*trans*11-18:2, RA) are products of C18 PUFA biohydrogenation in the rumen (Laverroux, Glasser, Gillet, Joly, & Doreau, 2011). Bacteria in the gut of ruminant animals also produce methyl-branched chain FA (*iso* and *anteiso* FA, BCFA) by deamination and elongation of branched amino acids (Val, Leu and Ile) (Vlaeminck, Fievez, Cabrita, Fonseca, & Dewhurst, 2006). All these FA can reach the mammary gland where they are incorporated into dairy lipids. Because their main dietary source are dairy products, they have been proposed as biomarkers of dairy fat intake (Berriozabalgoitia et al., 2021). Besides, these FA have been related to beneficial health effects. For example, RA has been related to reduced risk of cancer, atherosclerosis and obesity (Burdge et al., 2005) and BCFA have been shown to have anti-cancer activity (Vlaeminck et al., 2006).

On the other hand, olive oil is the main fat in the Mediterranean diet, its composition of FA is well defined and its favourable effects on human health have been widely demonstrated.

Animal models are important to understand the physiological and metabolic mechanisms of pathological states in which lipid metabolism is involved. Most of lipid metabolism comparisons between species are primarily focused on plasma lipoprotein profiles and major lipid components such as total cholesterol (TC) and TG (Kaabia et al., 2018; Yin et al., 2012). In these studies, hamsters were shown to be the animal model with a lipid metabolism most similar to that of humans.

Golden Syrian hamsters (*Mesocricetus auratus*) began to be used in the 1980s to study diet-induced atherosclerosis and cardiovascular disease in humans. Although not yet widely used today, they are a suitable model for research into diseases of this type, as they tend to suffer from hypercholesterolemia and atherosclerosis early lesions with an atherogenic diet (Nistor, Bulla, Filip, & Radu, 1987). Moreover, hamsters and human lipid profiles are comparable and both share CE transferase protein (CETP). This protein facilitates the transport of CE and TG between lipoproteins (Kaabia et al., 2018). However, very few scientific works described in detail the FA composition of plasma and erythrocytes in hamsters, and none work was found comparing them with that described in humans.

The FA composition of dairy products and olive oil is very different. Yet, both are habitual components of the human diet. Thus, the comparison of their effect on plasma and erythrocytes FA, when they are ingested as part of an equilibrated diet in healthy subjects, is interesting in order to understand the metabolic fate of different kind of FA, and to analyse whether, in this aspect of lipid metabolism hamsters perform in similar way than humans.

2. Materials and methods

2.1. Hamsters, diets and experimental design

Experiments with hamsters were carried out in accordance with the institution's guide for the care and use of laboratory animals (approval document reference CEBA/209/2011/VIRTO LECUONA).

Four-week-old male Golden Syrian Hamster (*Mesocricetus Auratus*) RjHan:AURA (Janvier Europe, France) (n = 16) were housed in controlled room temperature and humidity and under a 12:12 h artificial light/dark cycle (light on at 21:00) with free access to water and food. After a week adaptation period, the hamsters were randomly distributed in two experimental groups of eight animals each, two animals in each cage.

Each group followed an experimental diet for 14 weeks. Basal mix diets were prepared by Harlan (Teklad Custom Research Diet, Harlan Laboratories, Madison, WI, USA) and were supplemented with olive oil (OO7 diet) or milk fat (MF7 diet) to obtain a final concentration of 7% of fat by weight. Commercial olive oil was purchased from local market (Virgin Olive Oil, La Española, Acesur, Spain). Milk cream was obtained by centrifugation (2000 g at 4 °C for 30 min) of raw sheep milk purchased from a local sheepherder. Sheep milk was used because of its higher content of fat and FA as VA and RA comparing with cow milk. General composition of diets and FA composition of used fats are shown in Table 1 and Supplementary Table 1, respectively.

Faeces were collected for 3 consecutive days immediately prior to the end of the study and stored at −80 °C until analysed. Hamsters were feed deprived for 12 h and anesthetized with isoflurane (100% w/w, Esteve, Barcelona) before sacrifice. Blood samples were collected by cardiac puncture using capillary tubes, with EDTA as anticoagulant. Plasma and erythrocytes were separated by centrifugation at 800 g during 30 min. After separation, samples were kept frozen at −80 °C until analysed.

2.2. Human study

Samples of plasma and erythrocytes were obtained from the intervention study previously described (Berriozabalgoitia et al., 2021). Briefly, participants in the study were asked to follow their habitual diet but with no dairy products during 18 days (no dairy diet, NDD). At the end of the 18 days, and for another 18 days, subjects were asked to continue with their habitual diet adding at least 375 g of full fat dairy products and recording the amount of dairy products ingested every day (dairy rich diet, DRD). The intervention study was conducted according to the guidelines of the Declaration of Helsinki, and approved by the Ethics Committee of the University of the Basque Country (protocol code CEISH/199/2013/ VIRTO LEKUONA). All participants signed the Informed Consent document prior to the start of the study.

Blood samples were collected after overnight fasting at the end of each period, in 5 mL vacuum tubes impregnated with EDTA. Plasma and erythrocytes were separated by centrifugation at 800 g during 30 min. After separation, samples were kept frozen at −80 °C until analysed.

2.3. Fat extraction and FA analysis

A modified Folch method was used to extract fat from cream, olive oil and faeces. Briefly, 1 g of sample was dispersed in 40 mL chloroform: methanol: water (2:1:1). In the case of faeces, samples were ground in a mortar and homogenized with the solvent mixture in a potter homogenizer. The chloroform phase was separated by centrifugation (2200 g, 15 min, 4 °C) and washed twice with 25 mL of deionised water. The

Table 1
General composition of diets.

	OO7[1]	MF7[2]
Protein (g/kg)	180.8	180.6
Carbohydrates (g/kg)	511.5	511.7
Fat (g/kg)	70.0	70.4
Fiber (g/kg)	64.6	64.6
Energy (kcal/g)	3.4	3.4
Protein (% kcal)	21.3	21.2
Carbohydrates (% kcal)	60.2	60.1
Fat (% kcal)	18.5	18.6
Cholesterol (mg/kg)	157	155

[1] Diet containing 7% (w/w) of olive oil. [2]Diet containing 7% (w/w) of milk fat.

chloroform was removed under vacuum and the extracted fat was weighed. Extracted fat was then dissolved in toluene and glycerides were transesterified to the corresponding FA methyl esters (FAME) by a solution of sodium methoxide in methanol as described by Collomb and Bühle (2000).

Fat extraction from plasma and erythrocytes, both from humans and hamsters, and TFA methylation were accomplished in one-step, following a modified method of Bondia-Pons (Bondia-Pons, Moltó-Puigmartí, Castellote, & López-Sabater, 2007). FAME were prepared from 200 μL of plasma by sequentially adding 2.5 mL of 0.5 M sodium methoxide in methanol followed by 2.5 mL of 14% boron trifluoride in methanol. Resulting FAME were extracted adding 1.0 mL n-hexane and collected in a vial with anhydrous sodium sulphate. For erythrocytes, after adding sodium methoxide, the cell suspension was sonicated for 3 min in 10 s cycles.

FAME separation was achieved by gas chromatography on a 100 m CpSil88 capillary column (Varian Inc.). The chromatograph (Agilent 7890A Chromatograph, Agilent Technologies) was equipped with a FID detector. FAME were separated as described by Collomb and Bühle (2000) and identified by comparing the retention times of the obtained peaks with those of authentic standards. Internal standard method was used to quantify the amount of each compound, with undecanoic (11:0), tridecanoic (13:0) and nonadecanoic (19:0) acids as internal standards. The absolute concentration of FA was expressed in μmol/L and, from this, the molar percentage was calculated.

Stearoyl-CoA desaturase 1 (SCD-1) activity was estimated using indices based on the product to precursor FA ratios 16:1n-7/16:0 or 18:1n-9/18:0 in plasma and erythrocytes fat (Vessby, Gustafsson, Tengblad, & Berglund, 2013).

2.4. Plasma cholesterol, TG, and glucose measurements

Plasma biochemical parameters were analysed by colorimetric enzymatic assays, using commercial kits: fasting glucose, TG and TC by Biosystems kits (Biosystems, Barcelona, Spain) and Wako kit for free cholesterol (Wako Chemicals, Richmond, VA). CE were calculated by subtracting free cholesterol from TC.

2.5. Statistical analysis

Data were expressed as mean ± SEM. Studeńs T test was used to compare means for two groups, after checking for homogeneity of variance using Levene's test. Statistical significance was declared at P < 0.05. All analyses were done using the IBM-SPSS statistical software for Windows, version 25 (IBM, Chicago, Ill, USA).

3. Results

3.1. Hamsters

The performance of hamsters fed experimental diet based on olive oil (OO7) or milk fat (MF7) was similar and no statistical difference was found in food and energy intake, weight gain and feed efficiency (Table 2). Total plasma cholesterol and CE were slightly, but significantly, higher in OO7 hamsters.

3.2. FA in food and hamster faeces

The profile of FA of both type of food is very different (Fig. 1A, Supplementary Table 1). Main FA group in olive oil corresponds to *cis* MUFA (c-MUFA) (77 mol%), while milk fat contains SFA in the highest proportion (30% of medium chain SFA, MCSFA and 40% of long chain SFA (LCSFA)).

The concentration of fat in faeces was similar in both animal groups (Table 2). FA composition of food and faeces were compared in order to determine the absorption efficiency of different type of FA. Main FA

Table 2
General physical and plasma biochemical parameters of hamsters.

	Hamsters			
	OO7[1]	MF7[2]	SEM	P
General performance				
Initial weight (g)	87.52	90.74	1.960	0.429
Final weight (g)	117.5	121.0	3.705	0.656
Weight gain (g)	32.48	33.36	2.639	0.876
Food intake (g/d)	7.489	7.446	0.1590	0.897
Energy intake (kcal/d)	25.46	25.32	0.5407	0.897
Fat in faeces %	1.665	1.463	0.09002	0.353
Plasma biochemistry				
TC (mmol/L)	3.764	3.457	0.07418	0.005
CE (mmol/L)	3.017	2.659	0.1043	0.008
TG (mmol/L)	0.4700	0.5733	0.03371	0.133
TFA (mmol/L)	8.711	6.059	0.8862	0.136
FA in CE (%)	39.94	44.43	3.588	0.237
FA in TG (%)	16.65	29.37	3.720	0.008
Glucose (mmol/L)	8.515	8.209	0.1392	0.323

[1] Hamsters fed the diet containing 7% (w/w) of olive oil. [2]Hamsters fed the diet containing 7% (w/w) of milk fat. CE: Cholesteryl esters; FA: Fatty acids; TC: Total Cholesterol; TFA: Total FA; TG: Triglycerides.

groups in faeces are shown in Fig. 1B. Detailed FA composition is shown in Supplementary Table 1.

The FA profile of the stool was more similar to each other than that of food (Fig. 1B). The molar concentration of c-MUFA was much lower in faeces than in food in both group of animals, which indicated that they were preferentially absorbed. LCSFA in faeces were in similar proportion as in food. On the contrary, PUFAn-6 and PUFAn-3 were detected in faeces of both animal groups in higher proportion than in their respective foods. Some FA were found in faeces but not in food. For instance, MCSFA, BCFA, *trans*-MUFA (t-MUFA) and conjugated linoleic acids (CLA) were detected in faeces of hamsters fed olive oil, almost in the same concentration than in those fed milk fat, although their concentration in the food was very low.

Worth mentioning individual FA are LA, which concentration was much higher in faeces (26.90% and 14.29% in hamsters of OO7 and MF7 group, respectively) than in food (6.07% and 1.88% in olive oil and milk fat, respectively). Docosahexaenoic acid (22:6n-3, DHA) was not detected in any of the foods, but it did appear in faeces in a significant proportion (3.87% and 8.19%, for OO7 and MF7, respectively). The proportion of VA, which is very low in olive oil (0.00136%), was higher in faeces of OO7 (5.72%) group than in the MF7 group (2.85%).

3.3. FA in plasma of hamsters

The concentration of TFA in the plasma of hamsters, calculated as the sum of the concentration of individual FA, were 8711 ± 1180 μmol/L and 6059 ± 999.4 μmol/L for hamsters of the OO7 and MF7 groups, respectively. There was no significant difference (P > 0.05) between both animal groups (Table 2).

The FA profile of plasma TFA was very similar in both groups of animals, regardless the type of ingested fat. As it can be observed in Table 3, PUFAn-6 were the main FA group (40 mol%), while the sum of LCSFA and c-MUFA were in similar proportion (26–28%). Only the concentration of the sum of MCSFA was significantly higher in hamsters fed milk fat than in those fed olive oil.

In both groups of animals the FA present in the highest concentration was LA (25.7 and 28.8 mol% in OO7 and MF7 groups, respectively), following by OA (24.1 and 21.8 mol%) and palmitic acid (18.8 and 19.8 mol%). No statistical significant difference was found between animal groups in the concentration of the main individual FA. The only exceptions were stearic (18:0), *cis*-vaccenic (*cis*11-18:1) and arachidonic acids (20:4n-6, ARA) whose concentration were slightly but significantly higher (Table 3) in OO7 group, and palmitoleic acid (*cis*9-16:1) that was in higher percentage in MF7 group. In relation to minor individual FA
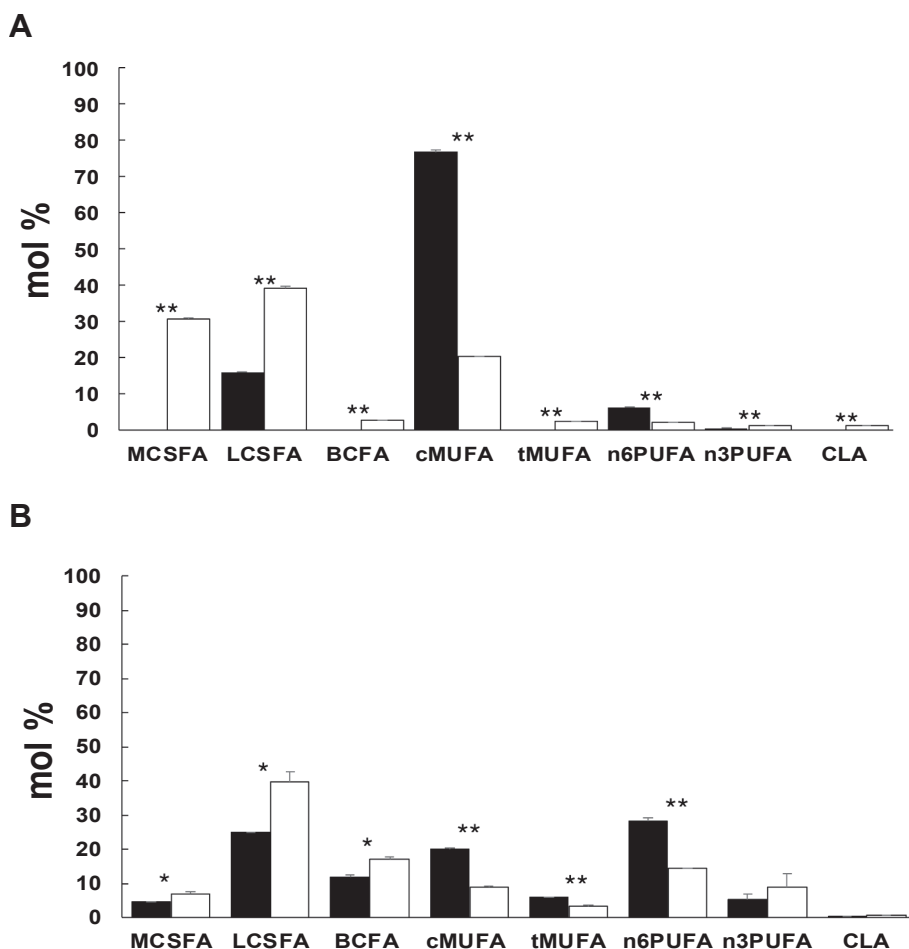
Fig. 1. FA composition (mol%, mean values + SD) of diets (A) and faeces of hamsters (B). FA are grouped in categories: Medium-chain saturated FA (MCSFA); long chain saturated FA (LCSFA); methyl-branched FA (BCFA); *cis*-monounsaturated FA (cMUFA); *trans*-monounsaturated FA (tMUFA); n-6 polyunsaturated FA (n6PUFA); n-3 polyunsaturated FA (n3PUFA); conjugated linoleic acids (CLA). In panel A black bars correspond to 7% (w) olive oil diet (OO7) and white bars correspond to 7% (w) milk fat diet (MF7). In panel B, FA of faeces samples from hamsters fed OO7 (black bars) or MF7 (white bars). Asterisks show significant differences: *, P < 0.05; **, P < 0.01; ***, P < 0.001.

(present in concentrations < than 1%, Table 3), significant differences were found in the percentage of 14 FA. Some of these differences can be attributed to their higher concentration in the diet fat (e.g., 12:0, iso16:0, *trans*-palmitoleic, VA or eicosapentaenoic acid (20:5n-3, EPA) acids in milk fat, or γ-linolenic acid (18:3n-6) in olive oil, Supplementary Table 1).

Moreover, the proportion of some BCFA, *trans*-FA and CLA, whose proportions were below 0.1% in the ingested fat, especially in olive oil, and are not synthetized by mammals, were found in plasma in significant proportions.

3.4. FA in erythrocytes of hamsters

The FA composition of erythrocytes in hamsters fed different fats, classified in FA groups is shown in Fig. 2A. Detailed FA composition is reported in Supplementary Table 2. When analysed by groups, FA profile was very similar in both animal groups. The main FA groups were PUFAn-6 (53.54% and 53.16% for OO7 and MF7 hamsters, respectively) and LCSFA (19.67% and 19.57%). There was no significant difference in these FA groups between animals. c-MUFA proportion (19.84% and 17.41%, respectively) was slightly, but significantly, higher in hamsters of OO7 group.

However, significant differences were found in minor FA (in groups and individually). Moreover, erythrocyte FA composition in hamsters seems to be more sensible to change in food fat than plasma FA, because of the 40 FA detected in erythrocytes, the proportion of 30 changed depending on the fat in the diet. The sum of MCSFA, BCFA, t-MUFA and CLA were significantly higher in erythrocytes of hamsters of MF7 group.

Among individual FA, twenty-one FA were in higher proportion in MF7 group than in OO7. These included all MCSFA, most BCFA, α-linolenic acid (18:3n-3, ALA), EPA and most CLA (Supplementary Table 2). All these FA were also in higher proportion in milk fat than in olive oil (Supplementary Table 1). FA whose percentage was higher in OO7 hamsters erythrocytes included OA, *cis*-vaccenic acid and ARA, which are also in higher proportion in olive oil. DHA was in the same proportion in both groups.

3.5. Humans

Diets and baseline characteristics of participants in the human study were published previously (Berriozabalgoitia et al., 2021). No difference were found in biochemical parameters in participants after following both diets (Table 4).

3.6. FA in human plasma

FA concentration in plasma samples of participants in the human intervention study after following NDD and DRD diets was 9778 ± 1643 and 10849 ± 1871 μmol/L, respectively. No significant difference was found between diets (Table 4). Results of main FA groups and data of individual FA are shown in Table 3. Main FA group were PUFAn-6 (44–42 mol%), following by LCSFA (28–26 mol%) and c-MUFA (around 22 mol%) in all participants. With respect to FA groups, small but significant differences were found in the concentration of the sum of MCSFA, LCSFA and CLA when the diet of the participants changed from NDD to DRD (Table 3).

Table 3

Fatty acid (FA) concentration means (mol%) in plasma samples.

FA	Hamsters				Human			
	OO7[1]	MF7[2]	SEM	P	NDD[3]	DRD[4]	SEM	P
MCSFA								
10:0	0.3017	0.4085	0.03329	0.075	0.2805	0.3112	0.009159	0.094
12:0	0.1209	0.2565	0.03963	0.012	1.095	1.077	0.03796	0.818
14:0	0.2844	0.5941	0.1124	0.204	0.9390	1.420	0.05673	0.000
15:0	0.08550	0.08821	0.002072	0.624	0.3386	0.3261	0.01020	0.549
Sum	0.7925	1.348	0.1674	0.043	2.653	3.135	0.08764	0.004
LCSFA								
16:0	18.85	19.81	0.5355	0.484	19.07	20.61	0.2836	0.005
17:0	0.3678	0.4226	0.01784	0.113	0.1921	0.2269	0.005486	0.001
18:0	7.234	6.126	0.3256	0.018	6.262	6.226	0.1013	0.859
20:0	0.03933	0.06024	0.00604	0.000	0.05709	0.04835	0.002053	0.031
21:0	0.02730	0.02100	0.00194	0.070	0.02311	0.02501	0.001402	0.506
22:0	0.4373	0.1610	0.08443	0.055	0.1423	0.1573	0.01673	0.660
24:0	0.01141	0.00952	0.00176	0.674	0.4135	0.4695	0.05877	0.640
26:0	0.04700	0.1490	0.02946	0.000	0.1690	0.1734	0.003800	0.337
Sum LCSFA	27.02	26.76	0.4260	0.826	26.33	27.94	0.2798	0.003
Sum SFA	27.81	28.11	0.4599	0.831	28.99	31.07	0.3323	0.001
BCFA								
iso14:0	0.01201	0.01512	0.00090	0.013	0.01704	0.01571	0.000698	0.350
anteiso14:0	0.01571	0.01794	0.00215	0.703	0.1133	0.1070	0.03115	0.922
iso15:0	0.05683	0.001271	0.01308	0.028	0.02060	0.04315	0.003469	0.001
anteiso15:0	0.01622	0.02881	0.00525	0.307	0.08240	0.02070	0.001397	0.000
iso16:0	0.04899	0.07687	0.00853	0.019	0.04034	0.06334	0.002415	0.000
anteiso16:0	0.006033	nd	0.00176	0.013	0.00555	0.00441	0.000317	0.074
iso17:0	0.3780	0.5019	0.05403	0.338	0.06532	0.1237	0.006279	0.000
anteiso17:0	0.4279	0.1081	0.09302	0.007	0.3430	0.2821	0.008854	0.000
Sum	0.9728	0.7868	0.08062	0.334	0.6134	0.6602	0.03974	0.454
c-MUFA								
cis9-14:1	0.3318	0.5072	0.05359	0.055	0.1646	0.2647	0.009999	0.000
cis9-16:1	1.494	2.331	0.2456	0.016	1.229	1.247	0.07653	0.908
cis10-17:1	0.1365	0.3470	0.06081	0.001	0.1084	0.09964	0.002826	0.122
cis6-18:1	nd	0.09561	0.02812		0.00966	0.03752	0.002774	0.000
cis9-18:1	24.08	21.77	0.9600	0.304	17.83	17.52	0.5337	0.774
cis11-18:1	2.071	1.546	0.1570	0.036	1.481	1.212	0.03397	0.000
cis11-20:1	0.1408	0.06092	0.02300	0.099	0.1081	0.09413	0.004018	0.081
cis13-22:1	0.04174	0.03773	0.00338	0.313	0.9235	1.110	0.04286	0.027
Sum	28.30	26.70	0.7361	0.372	21.85	21.59	0.5719	0.817
t-MUFA								
trans10-15:1	0.01122	nd	0.00324		0.01549	0.01597	0.000482	0.629
trans9-16:1	0.02592	0.2181	0.05680	0.023	0.01874	0.02064	0.001302	0.472
trans9-18:1	0.07440	0.05905	0.01086	0.593	0.2074	0.1654	0.09567	0.026
trans11-18:1	0.05533	0.1346	0.02444	0.063	0.03410	0.06887	0.003756	0.000
Sum	0.1667	0.4118	0.07691	0.080	0.2757	0.2709	0.01148	0.835
PUFA								
18:2n-6	25.71	28.77	1.043	0.153	33.40	32.36	0.7815	0.515
18:3n-6	0.9268	0.3476	0.1694	0013	1.248	1.271	0.07613	0.882
18:3n-3	0.07681	0.1386	0.02109	0.155	0.3365	0.3916	0.02232	0.222
20:4–6	13.16	11.52	0.4806	0.015	9.280	8.595	0.2651	0.200
20:5n-3	0.06990	0.1988	0.03725	0.001	0.3046	0.2878	0.01051	0.432
22:6n-3	2.615	2.456	0.1258	0.635	3.390	3.123	0.1284	0.304
PUFAn-6	39.79	40.63	0.6307	0.615	43.93	42.23	0.6856	0.221
PUFAn-3	2.762	2.793	0.1270	0.929	4.031	3.803	0.1311	0.390
Sum PUFA	42.55	43.50	0.1336	0.593	47.96	46.03	0.6583	0.146
n-6/n-3	14.42	14.70	0.6633	0.880	11.40	11.60	0.4390	0.827
CLA								
*cis9,trans11*CLA	0.05111	0.3090	0.09702	0.233	0.04986	0.1199	0.007336	0.000
*trans10,cis12*CLA	0.03555	0.02911	0.00297	0.380	0.06715	0.05770	0.005337	0.383
*cis9,cis11*CLA	0.08300	0.1205	0.01225	0.115	0.09198	0.09397	0.003910	0.803
*trans9,trans11*CLA	0.03021	0.03172	0.00454	0.902	0.02939	0.03992	0.02553	0.037
Sum	0.1998	0.4902	0.1119	0.251	0.2384	0.3115	0.01171	0.001
SCD-1 indices								
16:1/16:0	0.07960	0.1177	0.01142	0.038	0.0627	0.0602	0.00308	0.693
18:1/18:0	3.334	3.555	0.1456	0.561	2.903	2.850	0.1090	0.811
cis9,t11CLA/								
t11-18:1	0.9175	2.174	0.4896	0.259	1.523	1.784	0.07801	0.095

[1] Hamsters fed the diet containing 7% (w/w) of olive oil. [2]Hamsters fed the diet containing 7% (w/w) of milk fat. [3]Humans after non-diary diet. [4]Humans after dairy rich diet. BCFA: methyl-branched chain FA; CLA: conjugated linoleic acid; c-MUFA: *cis*-monounsaturated FA; LCSFA: long chain saturated FA; MCSFA: medium chain saturated FA; nd: not detected; SFA: saturated FA; SCD-1: Stearoyl-CoA-1 desaturase; t-MUFA: *trans*-monounsaturated FA.
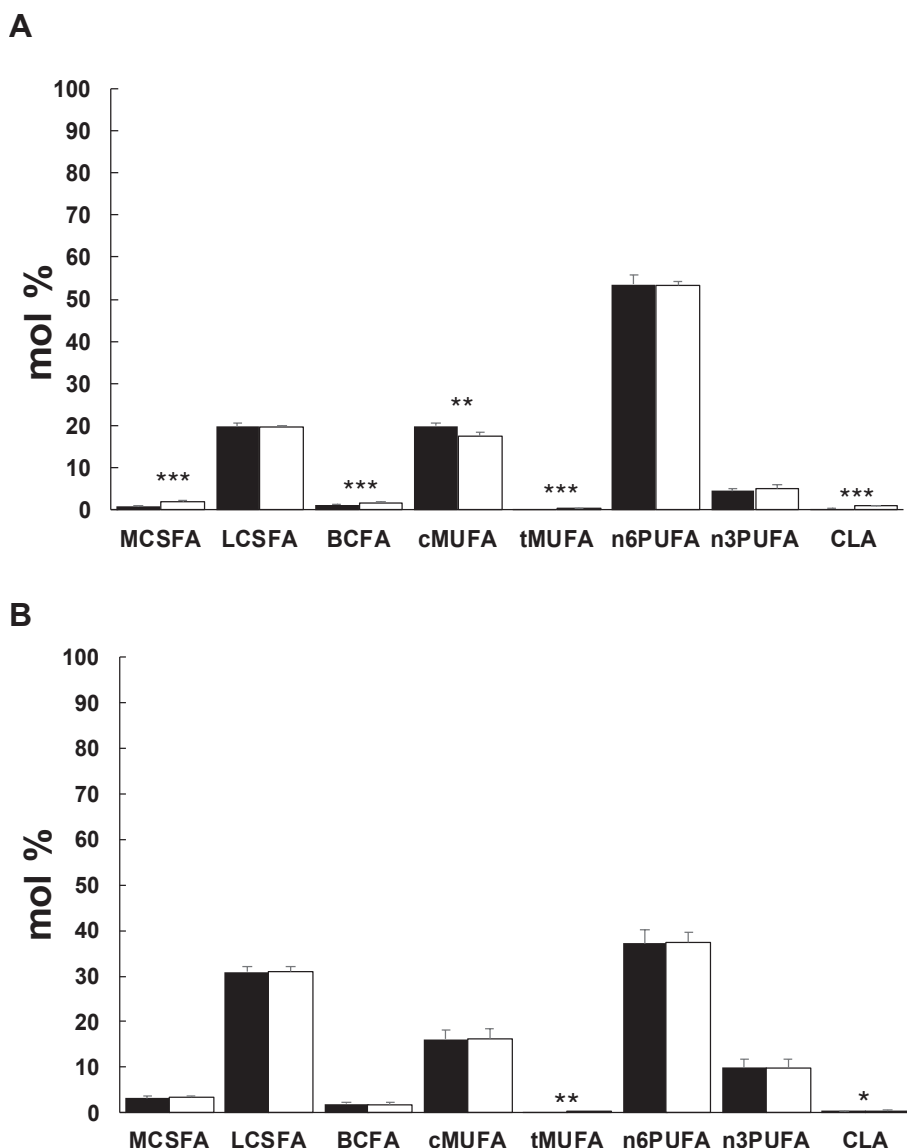
A

B

Fig. 2. FA composition (mol%, mean values + SD) of erythrocytes samples of hamsters (A) and humans (B). FA are grouped in categories: Medium-chain saturated FA (MCSFA); long chain saturated FA (LCSFA); methyl-branched FA (BCFA); *cis*-monounsaturated FA (cMUFA); *trans*-monounsaturated FA (tMUFA); n-6 polyunsaturated FA (n6PUFA); n-3 polyunsaturated FA (n3PUFA); conjugated linoleic acids (CLA). In panel A, black bars correspond to erythrocyte samples of hamsters fed a diet with olive oil7% (w) (OO7) and white bars correspond to hamsters fed 7% (w) milk fat diet (MF7). In panel B, black bars correspond to erythrocyte samples from participants in the intervention study after following a diet without dairy products, and white bars correspond to erythrocyte samples after following a diet rich in dairy products. Asterisks show significant differences: * P < 0.05; ** P < 0.01; ***; P < 0.001.

Table 4

Plasma biochemical parameters of human study.

	NDD1	DRD2	SEM	P
TC (mmol/L)	6.136	6.857	0.1517	0.097
CE (mmol/L)	5.030	5.620	0.1248	0.098
TG (mmol/L)	0.5462	0.5821	0.03555	0.905
TFA (mmol/L)	9.778	10.85	0.3916	0.177
FA in CE (%)	52.12	52.39	1.226	0.373
FA in TG (%)	16.75	15.82	0.7698	0.437
Glucose (mmol/L)	5.028	5.631	0.1290	0.110

Humans after non-diary diet. [2]Humans after dairy rich diet. CE: Cholesteryl esters; FA: Fatty acids. TC: Total Cholesterol; TFA: Total FA; TG: Triglycerides.

In plasma of humans following the two diets, FA present in the highest concentration was LA (33.4 and 32.4 mol% in NDD and DRD, respectively), following by palmitic acid (19.9 and 20.6 mol%) and OA (17.8 and 17.5 mol%). Among FA present in percentages higher than 1 mol%, myristic and palmitic acids were in significantly higher proportions after DRD and *cis*-vaccenic acid after NDD, in agreement with the higher proportions in their respective diets. Most differences were found in minor FA. Thus, four minor FA were in higher proportions in plasma of participants after NDD and ten FA in plasma of participants on

DRD. In the latter case, the increase can be attributed to their presence in dairy products (e.g., iso15:0, iso16:0, iso17:0, 17:0, VA and RA)

3.7. FA in human erythrocytes

The FA composition of erythrocytes in human samples, classified in FA groups is showed in Fig. 2B. Molar percentages of individual FA are collected in Supplementary Table 2. No statistical differences were found in main FA groups in human after both diets. PUFAn-6 constituted the main FA group (37 mol%.), following by LCSFA (31 mol%) and c-MUFA (16 mol%).

On the other hand, the sum of t-MUFA and CLA and the percentage of ten individual FA changed when the diet of participants changed from NDD to DRD. Nine of them were higher in erythrocyte samples after DRD and were significantly correlated with their increase in plasma and their presence in dairy fat (e.g., myristic acid, iso17:0, 17:0, VA and RA).

3.8. Comparative analysis

FA composition in hamsters' diet was controlled and known. However, in the human intervention study participants were asked to follow their habitual Mediterranean diet, avoiding any dairy product during

NDD period, or including a controlled amount of dairy products in DRD. This means that, in both periods, the participants in the human study ingested similar amounts of olive oil (25.2 ± 5.45 g/d) and other sources of FA, as vegetables, nuts, meat and fish. In spite of this, the differences found between the two species, following any diet, in relation to the main groups of FA in plasma were small. In both species, main FA groups were PUFAn-6 and LCSFA, which were in similar proportions in both species. c-MUFA proportion was slightly higher in hamsters than in human, even in animals fed milk fat, whereas PUFAn-3 and MCSFA were in higher proportions in humans.

NDD in humans can be considered equivalent to the OO7 diet in hamsters, since olive oil is the main source of fat in the Mediterranean diet. Comparing data of individual FA in plasma of these two groups, LA, OA and palmitic acid were the FA in the highest proportions in both, although LA was found in a higher percentage in humans than in hamsters, and the opposite occurred with OA, which is higher in hamsters. Differences were found between humans and hamsters in the percentage of other n-6 and n-3PUFA. All, except ARA, were in higher proportion in humans than in hamsters (Table 3). These differences were due, most probably, to the presence of foods that are the main source of these FA in the human diet, as vegetables, nuts and fish. Most other FA are in similar proportions.

With regard to the erythrocyte FA profile, it seems to be more characteristic of each species, with differences in percentages of major and minor FA between the two species, although in both PUFAn-6 constituted the main FA group. However, its proportion in hamsters was considerably higher than in humans, contrary to LCSFA whose percentage was much lower in hamsters (Fig. 2).

The effect of dairy fat ingestion on plasma and erythrocytes FA was different in hamsters compared to humans. In humans, the effect was similar in plasma TFA and erythrocytes FA, since in both type of samples a significant increase in the proportion of almost the same individual FA was detected. However, in plasma TFA of hamsters that were fed milk fat nine FA were in higher proportion than in the of OO7 group, but of those nine, only two (iso16:0 and petroselinic acid (cis6-18:1)) coincided with those that increase in humans after the DRD diet. In addition, the effect of milk fat consumption was more noticeable in hamsters erythrocytes than in humans, because the percentage of twenty-one FA was higher in MF7 group than in OO7, including all FA whose proportion were higher in human plasma and erythrocytes after DRD.

On the other hand, cis-vaccenic acid and anteisoheptadecanoic acid (anteiso17:0) seem to be related with olive oil intake, as their proportion were higher in plasma and erythrocytes of hamster of OO7 group than MF7 and in plasma of humans after NDD.

4. Discussion

FA found in fasting plasma are the complex results of various physiological processes related to lipid metabolism and reflect the nutritional and health state of the organism. Although hamsters have been long used as animal model for the analysis of lipid metabolism in humans, very few articles have analyzed in depth their plasma FA composition. Moreover, only one article (Yin et al., 2012) was found in which authors analyse the distribution of FA groups among plasma lipid fractions in various animal models in comparison to dyslipidemic humans. This work showed that non-human primates and normally fed hamsters are the best animal model in this regard. No similar comparison has been found for healthy subjects.

One process that can influence the plasma FA profile is the intestinal absorption of dietary fat. Faecal excretion has been used as a measure of the proportion of FA absorbed. However, the scientific literature describing the FA profile in faeces is scarce, either in experimental animals (Sugano & Imaizumi, 1995; Yokoyama et al., 2011) or in humans (e.g., McKimmie, Easter, & Weinberg, 2013; Neyrinck et al., 2021). FA excreted by hamsters depends partially on the FA content of ingested food. In hamsters, Sugano and Imaizumi (1995) showed that the faecal

excretion of FA in hamsters fed a diet rich in saturated FA tended to increase proportionally with the chain length of the FA, but the absorption was higher than 90% for all. Yokoyama et al. (2011) demonstrated a preferential excretion of SFA over unsaturated FA in hamsters fed diets with different proportions of both type of FA. Results of the present study are in agreement with those findings, as LCSFA appears to be absorbed proportionally to the amount found in food. To the contrary, c-MUFA are preferentially absorbed. Results in human studies (Neyrinck et al., 2021) showed similar results than in hamsters, with proportion of the main FA in faeces similar to that found in the present study.

However, it should be taken into account that faecal fat may include fat from food, as well as a fraction of the secreted bile lipids, mainly lecithin, bacterial lipids and lipids excreted by intestinal cells (Mu & Høy, 2004). Therefore, FA present in faeces are the result of a complex process that only can give an overall vision on FA absorption efficiency. Thus, the presence in faeces of significant amounts of BCFA, trans-FA and CLA, even in hamsters fed olive oil, indicates an important contribution of FA of microbial origin in hamsters. Hamsters possess a compartmentalized stomach, which consists of a forestomach and a glandular stomach (Marounek, Mrázek, Volek, Skřivanová, & Killer, 2016). The forestomach of erythrocytes and the rumen of ruminants are very similar, the microbiota is very abundant in it and can be the responsible of the production of the aforementioned FA. Moreover, the higher proportion of C18 PUFA in olive oil than in milk fat can explain the higher percentage of VA in faeces of hamsters of OO7 group, since these FA are the substrates for the microbial biohydrogenation process (Laverroux et al., 2011).

Some authors (Druart et al., 2015) have demonstrated the production of trans-FA and CLA in the gut of animals other than ruminants (as rats and rabbits). Neyrinck et al. (2021) also found trans-FA and CLA in human faeces in proportions similar to that found in hamsters in the present study and demonstrated their relationship with the presence of specific gut bacteria.

In the same way, the BCFA similar profile in the faeces of both group of animals support the microbial origin for most BCFA present in hamsters' faeces, since the BCFA profile in the gut seems to be more determined by the FA synthase activity of the microorganisms than by the precursor availability, at shown for ruminants ((Vlaeminck et al., 2006). Moreover, the higher proportion of some of these FA in faeces of MF7 group also shows the partial contribution of food intake.

As commented before, faecal fat may include a fraction of bile and bacterial lipids and lipids excreted by intestinal cells (Mu & Høy, 2004). These may be the source of the high proportion of PUFA found in hamster faeces compared to their presence in food.

Few scientific works described a detailed FA composition of plasma (Ishida et al., 2013; Sihag & Jones, 2018) or erythrocytes lipids (Bandarra, Lopes, Martins, Ferreira, Alfaia, Rolo, Correia, Pinto, Ramos-Bueno, Batista, Prates, & Guil-Guerrero, 2016; Morise et al., 2004) of hamsters. Besides, diets composition (in fat characteristics and percentages) varies widely among studies, which makes any comparison very difficult. Moreover, the number of individual FA determined in all cases was smaller than in the present study. Sihag and Jones (2018) analysed the plasma TFA of hamsters fed, among others, olive oil (10% weight). In this study, the main FA were found in percentages similar to ours, with some important exceptions. In Sihag's work c-MUFA are the main FA group and PUFA are in percentages similar to SFA. PUFAn-3 are in amounts similar to ours. Ishida et al. (2013) analysed only 13 FA in plasma of hamsters fed high fat diet (21%) without or with some PUFA added. In hamsters fed the control diet the FA are in similar percentages found in the present work.

Similarly, FA profile in erythrocytes of hamsters described in the literature varies among works and depending on the diet (Bandarra et al., 2016; Morise et al., 2004). In general, in the published works SFA are in a higher proportion than in ours, contrary to PUFAn-6, whose concentration is much higher in our work.

In human studies, the review of Hodson et al. (2008) shows that the profile of plasma FA of healthy people, with an equilibrated diet, is similar to that described in the present study when FA groups and main individual FA are compared. However, the same review (Hodson et al., 2008) also reports, in general, a higher proportion of SFA and lower of PUFAn-6 for human erythrocytes, although in some cases (Fuhrman et al., 2006) the composition resembles more the results of the present study. Erythrocytes constantly exchange FA in their membrane PL with those of plasma PL although their half-life is 28 days (Fuhrman et al., 2006). Differences in dietary PUFA intake could explain this variability in data because dietary PUFA incorporate into plasma PL faster and in higher proportions than MUFA or SFA (Hodson et al., 2008).

The FA profile of plasma and erythrocytes differs greatly from the profile of dietary fat. This may be because in fasting plasma the main lipoproteins (very low-density lipoproteins, VLDL) are produced in the liver, in which diet FA are diluted by endogenous liver FA. The incorporation of FA into the components of VLDL in the liver must be a deeply regulated process, directed by the specificity of enzymes implicated in the process. This process seems to be similar in hamsters and humans, since plasma TFA concentration (μmol/L) and FA profile in hamsters and humans following an equilibrated diet differ only slightly between the two species and is only partially influenced by the FA profile of the ingested fat.

The concentration of OA, palmitic and stearic acids are very different between diets. However, their concentration in plasma TFA differs very little, both in humans and in hamsters. OA and other non-essential FA as palmitic and stearic acids are incorporated mainly in TG (McCloy et al., 2004; Yin et al., 2012). Aarsland and Wolfe (1998) reported that OA was the predominant source of VLDL-TG synthesis in the liver compared to other FA. Similarly, Hodson et al. (2008) reported a significant higher amount of dietary OA compared to palmitic acid in VLDL-TG fraction. They explained that it is due to the specificity of the microsomal triglyceride transfer protein (MTP) in hepatocytes favouring MUFA incorporation during VLDL-TG synthesis. The same protein is involved in VLDL synthesis and secretion in hamsters (Gao, He, Ding, & Liu, 2010).

The origin of OA in liver can be dietary or "*de novo*" synthetized. The substrates of the enzyme responsible for the desaturation of FA in liver, SCD-1, can be "*de novo*" synthesized or dietary SFA (Rhee, Kayani, Ciszek, & Brenna, 1997). SCD-1 activity indices in plasma and erythrocytes are shown in Table 3 and Supplementary Table 2. In general, desaturase indices for stearic acid are higher than for palmitic acid and in hamsters higher that in humans, as also observed by Rhee et al. (1997). In any case, OA and palmitoleic acid found in plasma and erythrocytes either may come from food or be formed by the action of SCD-1 in the liver. As there is no difference in palmitoleic acid among hamsters' diets, the proportion of palmitoleic acid related to palmitic acid may reflect better the changes in SCD-1 activity. In hamsters, this index is higher in animals fed with milk fat. A study with humans (Vessby et al., 2013), comparing the effects of a diet based on butter fat with a diet containing MUFA fat, keeping all other dietary components constant, showed a higher SCD-1 activity index, calculated by the ratio palmitoleic to palmitic acids in CE, on a diet rich in butter fat than on a diet containing MUFA. The reason may be the fact that SFA are strong activators of SCD-1, as a defence mechanism against the negative effects of SFA in cells, as speculated by Mauvoisin and Mounier (2011). Miller and Ntambi (1996) highlighted the importance of maintaining the ratio of OA to stearic acid constant to maintain the membrane fluidity. Small changes in this ratio can affect the ability of the cell to respond to external stimuli. Because of that, it is a high-regulated ratio in humans, and seems to be also in hamsters, as 18:1n-9/18 index is similar in humans and hamsters and it does not change with diet. The production of OA from stearic acid, in order to maintain this ratio, may be the reason why the concentration of stearic acid was lower in the plasma of hamsters fed milk fat, although its concentration was higher in the food.

In the liver FA are incorporated mainly in TG, but also in PL and CE,

and released to the circulation in VLDL. FA in TG are more prone to be incorporated into organs and tissues to be oxidized or stored, while FA in PL and CE can stay longer in plasma lipoproteins (McCloy et al., 2004). As can be seen in Table 2, FA in CE accounts for around the 40% of TFA of plasma of hamsters, while FA in TG are the 17 and 29% of TFA (in OO7 and MF7 groups, respectively). Kaabia et al. (2018) compared plasma lipid concentration in humans with hamsters, among other animal models. They also found that in hamsters CE were in higher concentration than TG and that the concentration of CE was 10% higher in humans than in hamsters, as in the present work.

Yin et al. (2012) analysed the proportion of FA in different lipid fractions, taking into account their condition of non-essential, or essential, divided in n-6 and n-3 families in dyslipidemic humans and several animal models. They found great similarities to this respect between humans and normal-fed hamsters. They found that PUFAn-6 are the main FA in CE (64% of TFA), while PUFAn-3 were in PL (5%), TG (3%) and CE (2%). Other authors also demonstrated that PUFA are preferentially incorporated in CE and PL in humans (Hodson et al., 2008; McCloy et al., 2004). Greater acylation into plasma (and tissue) PL and CE could explain the greater whole-body retention of LA and other PUFA (McCloy et al., 2004) and their higher concentration in plasma and erythrocytes in comparison with their content in food. In the same way, as CE are in higher concentration in humans than in hamsters, this difference can explain the higher concentration of PUFA found in human plasma than in hamsters. This also can explain the presence of LA (and other PUFA) in faeces in relative high concentration, coming from enterocytes metabolism or from bile lecithin, as commented before.

In any case, the content of PUFA in plasma and erythrocytes seems to be highly regulated. PUFA content and n-6/n-3 ratios differed greatly between hamsters' diets, but no difference was observed in total PUFA proportion in plasma and erythrocytes. Bandarra et al. (2016), feeding hamsters with different combination of fat with various n-6/n-3 ratios, also observed that, although total n-3 and n-6 PUFA in erythrocytes varied depending on the diet, total PUFA proportion did not change. The main PUFAn-6 is LA and the main PUFAn-3 is ALA in both kind of dietary fat, but their proportions are very different (Supplementary Table 1). Both n-6 and n-3 FA are known to compete for common enzymes in the synthesis of longer and more unsaturated FA (long-chain PUFA, LCPUFA). LA and ALA are both substrates for microsomal delta-6 desaturase (D6D). However, this enzyme has a two- to three-fold higher affinity for ALA (Wien, Rajaram, Oda, & Sabaté, 2010). The main product of LA metabolism is ARA and the main products of ALA metabolism are EPA and DHA. EPA concentration in plasma and erythrocytes of hamsters fed milk fat was higher than in olive oil fed hamsters, consistent with a higher concentration of ALA in the milk fat. To the contrary, ARA proportion in both, plasma and erythrocytes was higher in animals fed olive oil, as the proportion of LA is three times higher in the oil. Morise et al. (2004) also found that EPA augmented in erythrocytes of hamsters when dietary supply of ALA increased, while DHA stayed constant, as in the present study. They explained that there is a complex balance between n-6 and n-3 PUFA as the result of two simultaneous mechanisms. On the one hand, the competition between ALA and LA for D6D causes that as the ALA/LA ratio increases, less LA becomes ARA. And, on the other hand, the increased availability of n-3 LCPUFA can lead to a decrease in n-6 LCPUFA in order to respect the physicochemical properties (e.g., fluidity and curvature) of membranes and lipoprotein particles. Moreover, Wien et al. (2010) mentioned that the limiting step in the metabolism of PUFAn-3 family is the membrane saturation with DHA. This argument can explain why in hamsters differences were found in individual n-6 and n-3 FA (especially in erythrocytes) but DHA percent stayed constant. In humans, there are also no differences in the concentration of DHA in each compartment.

VA and RA are in much higher concentration in dairy fat than in olive oil, where they are found only in trace amounts (Supplementary Table 1). However, their concentration in plasma and erythrocytes of hamsters and humans are in similar levels, although differences were

found between groups. They were also detected in similar concentration in faeces of all hamsters, as commented before. In human studies, it has been probed that the consumption of relative high amounts of dairy fat produced a significant increase in the concentration of VA and RA in plasma and erythrocytes (Berriozabalgoitia et al., 2021). RA:VA ratio is approximately 1:2 in the milk fat and 1:50 and 1:16 in faeces of OO7 and MF7 groups, respectively (Supplementary Table 1). However, in plasma and erythrocytes of both species RA is in higher concentration than VA in almost all cases. This can be due to the endogenous desaturation of VA to RA by SCD-1 activity, as demonstrated by Turpeinen et al. (2002) in humans and by Lock, Horne, Bauman, and Salter (2005) in hamsters. Moreover, Turpeinen et al. (2002) found great inter-individual differences, ranging from non-responders to conversion rates higher than 30%. This variability can be seen also in hamsters, whose mean values for VA and RA percentages are much higher in the plasma of MF7 group than in OO7 group, but there is no significant difference between them because of the high standard deviation value. In hamsters' erythrocytes, as the variability is lower, the differences are significant. In addition, it has been demonstrated that, when consumed in the diet, RA is incorporated in all lipid fractions, but preferentially in CE, while VA is preferentially incorporated in TG and cannot be found in CE (Burdge et al., 2005). This fact can also account for the higher concentration of RA than VA in plasma, as CE are in higher proportion in plasma than TG, as commented before. In summary, it can be concluded that VA and RA in plasma can have three sources: food, gut microbial metabolism and endogenous production of RA from VA by SCD-1 activity. Furthermore, when the dairy fat is the food source of these FA, its influence can be amplified because the high content in SFA of this fat increases SCD-1 activity. Santora, Palmquist, and Roehrig (2000) investigated the desaturation of VA in rats and reported that VA taken with food can increase the RA concentration useful for the body by 6–10 times. This can be the reason for the contradictory health effects of CLA when it is taken as supplement in comparison with enriched foods (Larsen, Toubro, & Astrup, 2003).

In the same way, BCFA are in higher concentration in milk fat than in olive oil, but appeared in plasma of hamsters and humans in similar percentages. These type of FA have been studied in the scientific literature in relation to their presence in food, especially in dairy products and food of ruminant origin (Vlaeminck et al., 2006) and have been detected in human specific tissues as skin or brain (Mika et al., 2016). Few works detected their presence in human plasma (Lin et al., 2020) and, to the best of our knowledge, besides our previous work (Berriozabalgoitia et al., 2021), only one (Mika et al., 2016) determined their concentration. The data obtained by these authors are in the same level of ours, and coincide in the fact that anteisoheptadecanoic acid is the BCFA that is present in the highest percent. No data for animal models have been found. In our previous work, we demonstrated that in human plasma and erythrocytes iso16:0 and iso17:0 can be used as biomarkers of dairy intake, as their concentration increases proportionally with the intake of dairy fat. In hamsters, despite being also produced in the intestinal tract, their presence in plasma and erythrocytes is as low as in humans, and the effect of milk fat intake on iso16:0 and iso17:0 concentration is more clearly observed in erythrocytes than in plasma, as it was commented for VA and RA. Morise et al. (2004) also found that in hamsters changes in response to modification in diet FA composition were more clearly seen in erythrocytes than in plasma lipids.

Petroselinic acid was also proposed as dairy intake biomarker for humans (Berriozabalgoitia et al., 2021), although it was not related before to the intake of these products. The results of the present study in hamsters confirm the reliability of this FA as a biomarker since it was only detected in samples (faeces, plasma and erythrocytes) of milk fat fed hamsters.

5. Conclusions

In conclusion, it was demonstrated that plasma TFA concentration

and FA group profiles are similar in humans and hamsters. Differences were found between both species in the percentage of some individual FA. These differences can be explained by differences in the dietary intake and differences in the proportion of TG, CE and PL fractions in plasma of both species. Changes in dietary FA intake causes similar changes in FA concentration in the plasma of both species and can be explained by the same metabolic processes.

The erythrocyte FA profile differs more between the two species, probably due to the characteristic PL composition of the erythrocyte membranes in each species. Furthermore, the FA profile of hamster erythrocytes is more sensitive to changes in dietary FA than plasma, because the proportion of a higher number of FA changed significantly in response to the change in dietary fat. One reason for this could be the greater variability in the data obtained in plasma samples, which, in turn, could be due to the more complex composition of plasma lipids.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.fochms.2021.100060.

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