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Introduction: Humans are exposed to nanoparticles from a variety of sources through a broad range of exposure ways since nanomaterials are increasingly used in different productive sectors. Titanium dioxide (TiO2) is enclosed in many consumer products including pharmaceuticals, cosmetics, and foods. TiO2 (E171) is daily ingested as mixed nano- and submicron-sized particles since it is approved as a white pigment in Europe in a variety of food products. Noteworthy, the relevant risk assessment has never been satisfactorily concluded and growing alarms for human hazards deriving from TiO2 exposure are incrementally reported.
Objectives: The objective of the present study was to establish conceivable mechanisms by which nano-sized TiO2 particles affect physiological function of the intestinal epithelium layer. The well-established Caco-2 cell line differentiated on permeable supports was used as a predictive model of the intestinal barrier due to its ability to naturally differentiate into polarized cells which resemble the intestinal architecture. The resultant system was adopted to investigate changes triggered by TiO2 nanoparticles in monolayer barrier since intestinal epithelial barrier is crucial for the maintenance of physiological function and the prevention of uncontrolled antigens trafficking.
Results: Exposure to nanoparticles disrupted the tight junctions-permeability barrier with a prompt effect detectable after 4h incubation time and wide effects on barrier integrity at 24h. Transport and ultrastructural localization of TiO2 nanoparticles were determined by ICP-OES, TEM and ESI/EELS analysis, respectively. Nano-sized particles were efficiently internalized and preferentially entrapped by monolayers. Storage of nanoparticles inside the cells affected enterocytes viability and triggered the production of pro-inflammatory cytokines, including TNF-alpha and IL-8.
Conclusion: Taken together these data indicate that nano-sized TiO2 particles exert detrimental effects on the intestinal epithelium layer.

A9
INTERPLAY BETWEEN THE TOXIC ALPHA-GLIADIN PEPTIDE 31-43 AND TYPE 2 TRANSGLUTAMINASE ENZYME IN CELIAC DISEASE

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Introduction: Celiac disease (CD) is a widespread enteropathy triggered by a diet containing cereals with gliadins in genetically predisposed individuals. Alpha-gliadin peptide 31–43 (p31-43) is considered the main responsible of the innate immune response in CD patients and type 2 transglutaminase (TG2) enzyme is involved in CD by enhancing gliadin immunogenicity. Evidence has been reported on a role of TG2 in modulate p31-43 uptake by intestinal cells; indeed, antibodies to TG2 specifically reduced both p31-43 uptake by cells and its biological activity. However, little is known about molecular mechanism underlying p31-43 uptake. We aim to investigate the effect of p31-43 on TG2 expression and activity into a model of skin-derived CD fibroblasts; furthermore we investigate whether cell surfaceTG2 could be directly responsible of p31-43 translocation into intestinal cells.
Methods: We analysed TG2 levels by PCR and western blot analysis and we monitored TG2 activity by a microplate assay using the pentylamin-biotine as substrate in skin-derived CD fibroblasts. To visualize probable complex between cell surface TG2 or membrane proteins and p31-43 we chemical cross-linked of p31-43 on intestinal cell surface proteins and next, pulled-down peptide-proteins complexes using antibodies raised against p31-43.
Results: We found that p31-43 stimulation induced TG2 activity more in skin-derived control fibroblasts than in CD cells. On the contrary, TG2 expression was more markedly induced in celiac cells than in control ones. We also found that that cell surface TG2 was not necessary for p31-43 internalization, even if it had a regulating role in the process.
Conclusions: We demonstrated that p31-43 did not behave as a classical ligand; indeed, membrane composition and organization, instead of a specific receptor protein, may have a major role in p31-43 internalization by cells. The interplay between p31-43 and TG2 has an important role in CD pathogenesis.

A10
CELLULAR AND SYSTEMIC ANALYSIS BASED ON POLYUNSATURATED FATTY ACIDS PROTECTIVE EFFECTS AGAINST INSULIN- RESISTANCE CONDITION

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Introduction: ω3 Poly-unsaturated Fatty Acids (PUFA-ω3) have a protective and therapeutic role to prevent insulin – resistance (IR). In this study, the protective effect was evaluated through: 1) serum parameters related to IR (HOMA index and apelin serum levels); 2) hepatic insulin signaling pathway markers (phosphorylated protein kinase B, p-Ser473-AKT/PKB); 3) endoplasmic reticulum (ER) stress marker (phosphorylated transcription factor p-eIF2α); 4) mitochondrial dynamics marker (Mitofusin 2, Mfn2).
Methods: These parameters were evaluated into 3 Wistar rats groups, so treated for 6 weeks: 1- N rats, treated with a standard diet (10.6% fats J/J); 2- L rats, treated with a high fat diet, rich in lard (40% fats J/J); 3- F rats, treated with a high fat diet rich in fish oil, major PUFA-ω3 source (40% fats J/J). Standard methods were used to analyse glucose and insulin serum levels and to determine HOMA index. ELISA assay was utilized for serum apelin levels. Hepatic p-Ser473-AKT/PKB, p-eIF2α and Mfn 2 levels were determined by western blot.
Results and conclusions: L group exhibited systemic and hepatic IR (as showed by increased HOMA index and p-Ser473-AKT content, respectively) associated with ER stress (as showed by increased p-eIF2α content). At the systemic level, F group showed reduced HOMA index associated with increased apelin serum level compared to L group. Furthermore, we observed increased hepatic insulin sensitivity (as showed by reduced p-Ser473-AKT content) associated to ER stress reduction (reduced p-eIF2α content) in F group compared to L group. A fundamental role seems to be played by Mfn2, that increased in F vs L group, preventing not only mitochondrial integrity, but also eIF2α phosphorylation. In this way, fish oil may have positive effect in the prevention of ER stress and IR onset.

A11
EFFECTS OF SOME NUTRACEUTICALS ON THE TPC1 THYROID CELL LINE

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The majority of thyroid carcinomas come from follicular cells and are defined as differentiated thyroid tumors (DTC) and the two histological subtypes are papillary CT and follicular CT. Curcumin has a wide variety of biological functions, currently, in the literature has considerable attention. The present work defines the role of curcumin on the modulation of gene expression of different cell markers and cell cycle modulation. The study was carried out using CURCUMA NATUREX and adding other nutraceuticals such as piperine and vit. And, in order to define the role of these in the modulation of gene expression of cell and tumor markers.
TPC-1 cells were the cellular model. Initially treated with the different turmeric extracts and examined the expression levels of markers (proliferative, inflammatory, antioxidant, apoptotic). Thereafter TPC-1 cells were treated with MIX of turmeric, piperine and vitamin E to understand its efficacy and biomodulation on thyroid papillary carcinoma. Treatment with the three different curcumin extracts shows