children with leukemia and 1 (11.1%) of a patient with a solid tumor.

The median vitamin D supply in children from 0 to 3 years old was 16.6 [9.7–21.7] ng/ml, from 4 to 10 years old – 19.8 [14.7–24.8] ng/ml, from 11 to 18 years old – 16.8 [10.5–17.2] ng/ml. Vitamin D deficiency (less than 20 ng/ml) was detected in 6 (54.6%) children under 4 years old, in 8 (50.0%) children from 4–10 years old and 7 (77.8%) adolescents of 11 years old and older ($p < 0.05$); insufficiency with the level from 20 to 30 ng/ml was detected in 3 (27.3%), 6 (37.5%) and 1 (11.1%) children, and the level of more than 30 ng/ml was found in 2 (18.1%), 2 (12.5%) and 1 (11.1%) children, respectively.

Conclusions in the south of Russia, the majority (86.0%) of children and adolescents with cancer have a 25 (OH) D level of less than 30 ng/ml. Level of 25 (OH) D did not significantly depend on the type of cancer. Adolescents with cancer are at risk for vitamin D deficiency (less than 20 ng/ml).

315 INTEGRATING SAFFRON METABOLOMICS INTO THE TREATMENT OF PEDIATRIC CANCERS

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10.1136/archdischild-2021-europaediatrics.315

Natural plant extracts are an important source of antitumor agents, and still provide promising approaches for discovering new drugs. *Crocus sativus* (saffron) is endowed with anticancer, differentiating, antioxidant and genoprotective properties. Its pharmacological properties are attributed to biologically active substances, crocins (CRCs) which are hydrophilic carotenoids. They are glycosyl-esters of the amphiphilic natural carotenoid crocetin (CRT), which exhibits extensive distribution and penetration through lipid bilayers. The hemisynthetic derivative dimethylcrocetin (DMCRT) is similar to CRT and is soluble in many organic solvents. With regards to safety, saffron and its constituents are considered practically non-toxic substances. The current research aims to study the in vitro cytotoxic effect of the natural carotenoids CRCs and DMCRT on a medulloblastoma cell line.

CRCs are diluted to nuclease and protease free water and DMCRT to 10% DMSO.

For the biological assays TE-671 medulloblastoma cells are incubated in 96-well plates at a range of concentrations of CRCs (0.18–22.85 mg/ml) and DMCRT (0.18–11.43 mg/ml) for 24, 48 and 72 hours. Analysis of cell viability is performed with Alamar Blue and MTT viability assays.

CRCs manifest a cytotoxic effect in a dose and time-dependent manner ($p < 0.001$ for exposed cells to any concentration at 24, 48 and 72 hours versus cells not exposed); as their concentration increases, cell viability is reduced for all time points. For the same concentration, as the time of exposure increases, the inhibitory effect is increased. The antiproliferative effect of DMCRT is less pronounced, observed only at concentrations higher than 5.71 mg/ml at 24 and 48 hours and higher than

1.43 mg/ml at 72 hours, whereas for lower concentrations the effect is not statistically significant. IC₅₀ values for each time point are calculated as 3.230, 2.14 and 1.72 mg/ml for

CRCs and 5.9, 5.6 and 3.712 mg/ml for DMCRT at 24, 48, and 72 hours, respectively.

The results of our study could afford the basis of research, regarding the use of natural carotenoids as an alternative solution to the toxicity of retinoids, especially for the vulnerable pediatric population and during pregnancy, while retaining the anticancer properties of retinoids.

Acknowledgements The research is co-financed through the Program 'Support for researchers with an emphasis on young researchers-cycle B' (MIS 5048464) AND The Foundation for Education and European Culture (IPEP).

316 INTEGRATING NON PSYCHOACTIVE PHYTOCANNABINOIDS AND THEIR CYCLODEXTRIN INCLUSION COMPLEXES INTO THE TREATMENT OF NEUROBLASTOMA

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10.1136/archdischild-2021-europaediatrics.316

The non-psychotropic cannabidiol (CBD), deriving from *Cannabis sativa* is endowed with anticancer, antioxidant and genoprotective properties, which along with its safe profile suggest it as a promising approach in cancer therapy. The low solubility of CBD hampers its therapeutic potential.

Cyclodextrins (CDs) are cyclic oligosaccharides used in pharmaceutical industry to incorporate apolar molecules inside their hydrophobic cavity, increasing their stability, water solubility and bioavailability.

CBD-inclusion complexes with CDs are a good nanomedicine-based formulation strategy to improve CBD's properties. The current research aims to study the potential cytotoxic effect of CBD and CBD-CDs complexes CBD-RMβCD (randomly methylated β-cyclodextrin) and CBD-HPβCD (hydroxypropyl-β-CD) on neuroblastoma cells.

CBD is diluted in 10% DMSO and CBD/CDs solutions are prepared by mixing solid CBD, solid CDs and dH₂O. Phase solubility studies are conducted to determine improvement in CBD's solubility from CDs' addition. For the biological assays SH-SY5Y and BE(2)-M17 neuroblastoma cells are incubated at a range of concentrations (0.03125–4 mg/ml) of CBD, CBD-RMβCD, CBD-HPβCD, RMβCD and HPβCD for 24, 48 and 72 hours. Analysis of cell viability is performed with Alamar Blue viability assay.

CBD's solubility is enhanced in the presence of both CDs. CBD and all CBD/CDs exert significant cytotoxicity in a dose and time-dependent manner; as their concentration and time of exposure increase, cell viability is reduced. The cytotoxic effect is more pronounced in cells exposed to CBD-HPβCD for all concentrations and time-points. RMβCD and HPβCD at the highest concentration of 4 mg/ml exert antitumor action per se. IC₅₀ values are calculated as 0.29, 0.21, 0.06 mg/ml for CBD, 0.046, 0.035, 0.03 mg/ml for CBD-RMβCD, and 0.029, 0.023, 0.021 mg/ml for CBD-HPβCD at 24, 48, and 72 hours, respectively for SH-SY5Y cells. For BE(2)-M17 cells IC₅₀ values are 0.3, 0.27, 0.19 mg/ml for CBD, 0.1655, 0.1644, 0.1534 mg/ml for CBD-RMβCD, and 0.1086, 0.1020, 0.071 for CBD-HPβCD at 24, 48, and 72 hours, respectively.