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A maternal diet enriched in fibre and polyphenols during pregestation, gestation and lactation has an intestinal trophic effect in both the dam and the offspring

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Abstract: Maternal diet during lactation, pregnancy or even before can influence the health of the baby; being the Mediterranean diet the one with the highest level of evidence due to its richness in fiber and polyphenols, among other bioactive components. This study investigated the impact of a diet rich in fiber and polyphenols (HFP diet) supplemented during pregestation, gestation, and lactation at intestinal level in both dams and their offspring. This diet had an intestinal impact in both pregnant rats and their offspring in terms of intestinal growth. Further research is required to elucidate the underlying mechanisms involved.

Keywords: Mediterranean diet; maternal diet; fibre; polyphenols; gut

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1. Introduction

Current research indicates the vital role of mother's dietary habits and nutritional well-being not only during pregnancy but also before conception and throughout lactation in the health of the fetus and infant, respectively [1]. Inadequate or excessive, as well as pre-pregnancy weight conditions, significantly influences various aspects of reproduction, including maternal and paternal fertility, conception, placental, embryonic, and fetal growth, and perinatal complications. These factors collectively contribute to suboptimal pregnancy outcomes for both the mother and the infant [2].

Additionally, nutrition during the first 1000 days of life (including pregnancy and the first two years when lactation is recommended by the World Health Organization (WHO)) [3], plays a pivotal role in a child's development. During this critical period, the baby's metabolic, immune, endocrine, and other developmental pathways mature concurrently with the establishment of symbiotic relationships with the microbiota [4].

The composition of the maternal diet is then of importance, and that aligned with Mediterranean Diet (MD), rich in fiber and polyphenols, among other components, seems to have a positive impact on both the mother's and the infant's health. However, this last aspect has been less studied. In addition, the specific period in which the dietary components can have their most significant impact on the fetus/infant still remains to be stablished [5].

Thus, the aim of the present research was to investigate the impact of a high-fiber and polyphenol-rich (HFP) diet, supplemented during pregestation, gestation, and lactation, on the body growth and the intestinal health of both dams and their offspring. Additionally, the study assesses its impact on plasma immunoglobulin concentrations.

2. MATERIAL AND METHODS

2.1. Animals

The study began with six-week-old female Wistar rats (N=18) upon their arrival from Janvier Labs (Saint-Berthevin, France), and housed in the experimental animal facility in the Diagonal-Campus of the Faculty of Pharmacy and Food Science (University of Barcelona, UB). The animals underwent a one-week acclimatization period before the start of the project. During the pregestation period, the rats were housed in pairs andduring gestation and lactation they were individually housed. The animals were kept under controlled environmental conditions, which included humidity (50–55%), temperature (21 ± 2 ºC), and 12-hour light-dark cycles, and *ad libitum* access to food and water. The procedures followed were approved by the Ethics Committee for Animal Experimentation of the University of Barcelona (Ref. 240/19) and the Generalitat de Catalunya (Ref.10933).

2.2. Diets and Experimental Design

The animals were distributed into two groups: a control group (REF group, n=9) that received the standard AIN-93G diet and another group (HFP group, n=9) that received a high-fiber and polyphenols diet. This diet was formulated based on the fiber and polyphenol content found in dietary profile of a gestating/lactating Spanish Mediterranean Cohort [6**]**. The 9-week study was divided into three periods: pregestation, gestation, and lactation, of 3 weeks each. After the pregestation phase, mating occurred for 4 days, resulting in 6 pregnant rats per group (n=6/group). Some pups from each litter were euthanized on day 1 (n=24/group), and later the litters were culled to 8 pups per mother. After the 3-week lactation period, mother rats and four pups per mother (n=24/group), equally distributed by gender, were euthanized. Throughout these 9 weeks, weight, food intake, and water consumption were monitored three times a week, and feces were collected weekly.

2.3. Sampling

The following organs were weighted after euthanizing the animals at each time point: spleen, stomach, cecum, small intestine, liver, right kidney, thymus, heart, salivary glands (salivary G), and brain. In the case of the small intestine, measurements of length and width were taken.

2.4. Statistical analysis

The Student-T test was used for statistical analysis. Significant differences were established at $p < 0.05$.

3. RESULTS AND DISCUSSION

3.1. Effect of HFP Diet on Maternal and Offspring Organ Weights

The impact of the HFP diet on organs weight is presented in Figure 1. It can be observed that the maternal diet did not affect most of the organs in neither the mothers or the infants. However, significant differences were observed in the relative weight of the cecum and the liver of the dams. Specifically, the HFP diet resulted in a notably higher cecum relative weight and a lower relative weight of the liver compared to the REF diet ($p < 0.05$). These or other changes were not observed in the pups from mothers receiving this diet on day 1, but on day 21, the effect of the maternal diet on the cecum was also evident ($p < 0.05$).

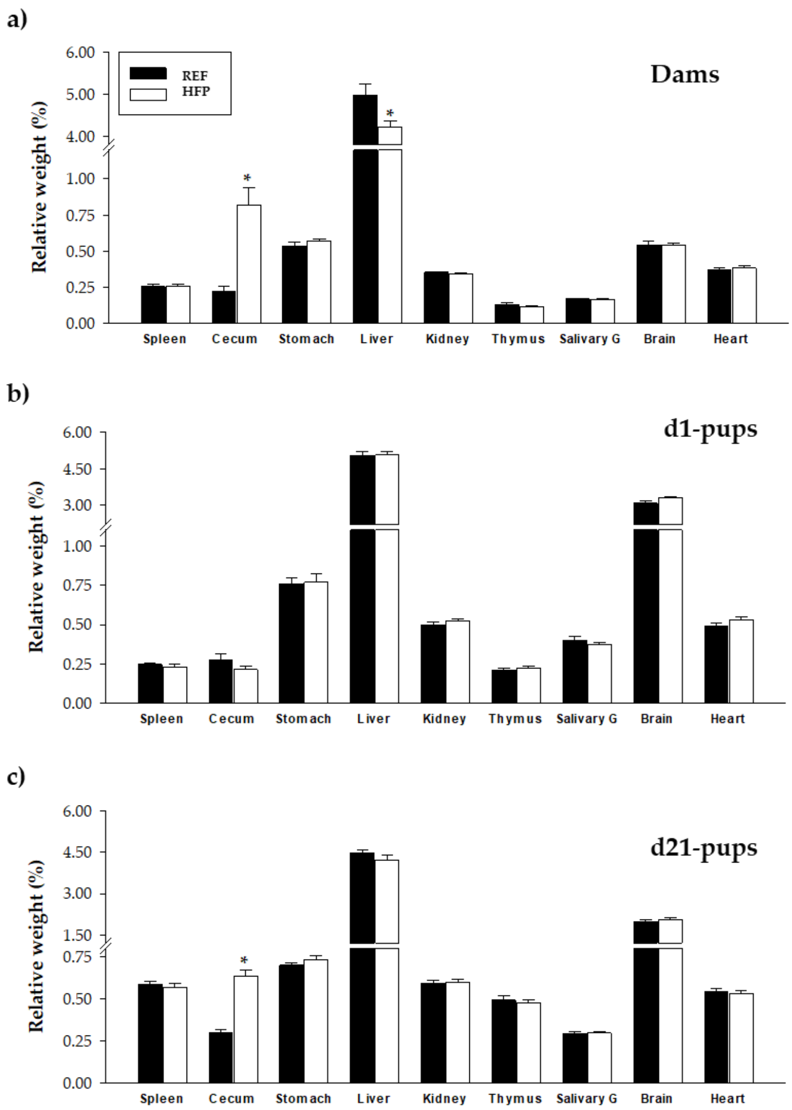

Figure 1. Relative organ weights (%) in high-fiber and polyphenols rich group (HFP) and reference group (REF) for (**a**) Dams; (**b**) d1-pups; and (**c**) d21-pups. Results are expressed as mean ± SEM of the g of organ per 100 g of body weight (n = 6/group for dams, n = 12/group in d1-pups and n = 24/group in the d-21 rats). Statistical differences: * $p < 0.05$ vs. REF.

The cecum, which is the initial segment of the large intestine located between the ileocecal valve and the ascending colon, serves as a reservoir for fecal storage and is the primary site for the fermentation of soluble fiber. It is known that soluble fiber reaches the colon undigested because of its resistance to enzymatic degradation. It can then be metabolized by the gut microbiota, leading to the production of short-chain fatty acids (SCFAs). It is plausible to suggest that the fiber derived SCFAs may induce the proliferation of beneficial bacteria such as bifidobacteria and lactobacilli, while inhibiting the growth of harmful bacteria. This fermentation process and the subsequent growth of beneficial bacteria could be the factors contributing to an increase in the cecal trophic effect and the fecal mass production [8]. Additionally, formation of viscous solutions due to soluble fiber combining with water may increase the volume of intestinal contents, potentially distending the walls of certain gastrointestinal tract structures.

3.2. Effect of HFP Diet on Maternal and Offspring Small Intestine

The small intestine of dams, d1- and d21-pups were evaluated for weight, length and width (Table 1). The weight of the intestine in dams and d1-pups was higher in the HFP group than in the REF group ($p < 0.05$), although this difference was not observed on day 21.

Table 1. Relative weight of the small intestine (SI, %) and measurements of small intestine length (cm) and width (cm) at the end of the nutritional intervention for all experimental groups. Data is expressed as mean ± SEM (n = 6/group for dams, n = 12/group for d1-pups and n = 24/group for the d-21 rats). Statistical differences: * $p < 0.05$ vs. REF.

	Dams		**d1-pups**		**d21-pups**	
	REF	**HFP**	**REF**	**HFP**	**REF**	**HFP**
SI weight (%)	3.31 ± 0.08	4.03 ± 0.11 *	3.11 ± 0.11	3.23 ± 0.07*	3.40 ± 0.06	3.78 ± 0.09
Length (cm)	88.54 ± 5.26	86.20 ± 4.98	17.82 ± 0.49	19.53 ± 0.42*	43.78 ± 1.54	52.65 ± 2.94*
Width (cm)	1.04 ± 0.05	1.18 ± 0.12	n.e.[1]	n.e.	0.53 ± 0.01	0.60 ± 0.06

[1] n.e.: non-evaluated.

In addition, the maternal HFP diet also influenced the length of the small intestine in the offspring at both 1 and 21 days of life compared to those from the REF group ($p < 0.05$). This trophic effect is unlikely to be related to the direct intake of the fiber or polyphenols. Instead, it may result from intrauterine epigenetic changes, the impact of the diet on maternal milk composition or microbiota, or a combination of these factors [9,10]. Future studies will evaluate the mechanisms involved to gain a better understanding of these results.

4. CONCLUSION

In conclusion, a diet rich in fiber and polyphenols appears to have an intestinal impact in both pregnant rats and their offspring. However, further research is required to elucidate the underlying mechanisms of these effects and their potential implications for maternal and neonatal health.

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Informed Consent Statement: Not applicable.

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Conflicts of Interest: The authors declare no conflict of interest.

References

1. Barker DJ. The developmental origins of adult disease.*J Am Coll Nutr* **2004**,*23(6 Suppl)*,588S-595S. doi: 10.1080/07315724.2004.10719428.
2. Marshall NE et al. The importance of nutrition in pregnancy and lactation: lifelong consequences. *Am J Obstet Gynecol* **2022** May;226(5):607-632. doi: 10.1016/j.ajog.2021.12.035
3. World Health Organization. WHO antenatal care recommendations for a positive pregnancy experience. Nutritional interventions update: multiple micronutrient supplements during pregnancy. *Geneva, Switzerland: World Health Organization*; **2020.**

4. Christian P, et al. Risk of childhood undernutrition related to small-for-gestational age and preterm birth in low- and middle-income countries. *Int. J. Epidemiol*. **2013**; *42:* 1340-1355. doi: 10.1093/ije/dyt109.
5. Lindsay KL, Buss C, Wadhwa PD, Entringer S. The interplay between nutrition and stress in pregnancy: implications for fetal programming of brain development. *Biol Psychiatry* **2019**; 85: 135–49 doi: 10.1016/j.biopsych.2018.06.021.
6. Selma-Royo M, García-Mantrana I, Calatayud M, Parra-Llorca A, Martínez-Costa C, Collado MC. Maternal diet during pregnancy and intestinal markers are associated with early gut microbiota. *Eur J Nutr* **2021**; 60(3): 1429-1442. doi: 10.1007/s00394-020-02337-7
7. Martínez Agustin, O., Daddaoua, A., & Suárez Ortega, M. Relaciones metabólicas tisulares en el ciclo de ayuda y reglamentación. Bases fisiológicas y bioquímicas de la Nutrición, En *Tratado de Nutrición*, Tomo 1: Editorial Médica Panamericana, España, 2017; Vol. 1, pp. 154–196.
8. Morales-Ferré C, Azagra-Boronat I, Massot-Cladera M, Tims S, Knipping K, Garssen J, Knol J, Franch À, Castell M, Rodríguez-Lagunas MJ, Pérez-Cano FJ. Effects of a Postbiotic and Prebiotic Mixture on Suckling Rats' Microbiota and Immunity. *Nutrients* **2021**; 13(9): 2975. doi: 10.3390/nu13092975.
9. Moossavi S, Miliku K, Sepehri S, Khafipour E, Azad MB. The Prebiotic and Probiotic Properties of Human Milk: Implications for Infant Immune Development and Pediatric Asthma. *Front Pediatr* **2018**; 6: 197. doi: 10.3389/fped.2018.00197.
10. Grases-Pintó B, Abril-Gil M, Torres-Castro P, Castell M, Rodríguez-Lagunas MJ, Pérez-Cano FJ, Franch À. Rat Milk and Plasma Immunological Profile throughout Lactation. *Nutrients* **2021**; 13(4): 1257. doi: 10.3390/nu13041257.