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# Evaluation of the taste, smell, and appearance of formulas used in the management of cow's milk protein allergy: A multicenter, prospective, single-blind, cross-sectional observational study (CONTEST-2)

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### Abstract

The main drawback of hypoallergenic formulas for cow's milk protein allergy (CMPA) is their low palatability. This study aims to examine the decisions made by mothers of infants diagnosed with CMPA and physicians regarding the taste of extensively hydrolyzed formulas (eHFs), amino acid-based formulas (AAFs), and rice-based formulas. This single-blind, multicenter study was conducted in nine pediatric allergy centers across Türkiye and included 181 pediatricians and 137 mothers of children with CMPA. Seven substitution formulas without added sweeteners or additional flavorings available on the market were tested: Two AAFs (Neocate-Numil<sup>®</sup>, Alfamino-Nestlé<sup>®</sup>), one AAF with synbiotics (Pregomin Syneo-Numil<sup>®</sup>),

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one AAF specifically designed to meet the nutritional and lifestyle needs of children over 1 year of age (Neocate Junior-Numil®), one synbiotic eHF (Aptamil Pepti Syneo-Numil®), and two rice protein-based formulas (Evolvia RP1-Montero® and Evolvia RP2-Montero®). A sensory evaluation was conducted using a single-blind protocol, following the methodology previously applied in the CONTEST-1 study. Neocate Junior-Numil® was the most preferred product in terms of taste, smell, and appearance, as rated by both mothers and physicians. It was the most preferred formula by both mothers (49.6%) and physicians (62.4%) in terms of taste. Aptamil Pepti Syneo-Numil® ranked second (32.8% for mothers, 42.0% for physicians), followed by Evolvia RP2-Montero® (23.4%) for mothers and Alfamino-Nestle® (22.1%) for physicians. The fact that both mothers and physicians most frequently preferred Neocate Junior-Numil® suggests that sensory characteristics of formulas used in CMPA management—such as taste, smell, and appearance—may play a decisive role in treatment adherence. This finding highlights the importance of considering not only nutritional adequacy but also acceptability when selecting a formula.

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## Introduction

Cow's milk protein allergy (CMPA), commonly encountered in early childhood, is a significant hypersensitivity reaction not only due to its clinical manifestations but also because of the behavioral challenges it poses in the feeding process. In exclusively breastfed infants, maternal elimination diets are generally sufficient; however, in formula-fed infants, the use of hypoallergenic formulas is necessary. The formulas used in the management of CMPA are classified into extensively hydrolyzed formulas (eHFs), amino acid-based formulas (AAFs), and formulas derived from plant-based protein sources. In recent years, formulas containing prebiotics, probiotics, or a combination of both (synbiotics) have also been used with the potential to support the development of oral tolerance by modulating the gastrointestinal microbiota.<sup>1,2</sup> The taste profile of these hypoallergenic formulas used in the management of CMPA varies significantly, primarily depending on the protein source, degree of hydrolysis, and the presence of lactose. These differences in taste directly influence infants' acceptance of the formula, and consequently, their adherence to the treatment.<sup>3,4</sup>

Sensory attributes such as taste, smell, and appearance—which collectively determine palatability—play a critical role in influencing sensory memory during infancy and thereby impact adaptation to formula feeding. This experience is not limited to the infant alone, but also affects how caregivers and healthcare professionals evaluate the formula. In the current literature, data on the sensory properties of hypoallergenic formulas are mostly presented in terms of their compositional characteristics, and comparative studies specifically addressing palatability are quite limited.<sup>3-8</sup> This represents a critical gap, as poor palatability may lead to formula refusal, reduced adherence, and ultimately compromised dietary management of CMPA. Furthermore, little is known about how caregivers and healthcare professionals perceive these sensory attributes and how such perceptions influence clinical decision-making in practice.

This study aims to evaluate the perceptions of healthcare professionals and caregivers regarding the palatability

of different hypoallergenic infant formulas and to assess how these perceptions influence formula selection in the management of CMPA.

## Materials and Methods

This is a multicenter observational research study conducted across Türkiye, involving pediatric physicians and mothers of infants diagnosed with CMPA who had used hypoallergenic infant formulas. Participants were asked to evaluate the taste, smell, and appearance of seven different hypoallergenic infant formulas. The study is a continuation of the multicenter project conducted in 2022, titled the CONTEST study (Comparison of tastes of available nutritional integrated or nonintegrated formulas for infants older than 1 year of age with cow's milk allergy: A multicenter, prospective, single-blind, cross-sectional observational clinical study).<sup>6</sup>

The study was conducted in nine hospitals across different regions of Türkiye, each with a dedicated pediatric allergy and immunology department, and all serving as tertiary care centers. A total of 181 pediatricians—each with 2-30 years of clinical experience—and 137 mothers of infants diagnosed with CMPA and using hypoallergenic infant formulas participated in the study.

Inclusion criteria for mothers:

- Mothers of infants who had been diagnosed with CMPA and received hypoallergenic formula feeding within the past 12 months
- No known food or drug allergy
- No impairment in taste or smell perception
- Not experiencing an acute upper respiratory tract infection at the time of evaluation.

Inclusion criteria for physicians:

- Actively practicing as a certified pediatric specialist for 2-30 years
- Familiarity with at least two different brands of infant formulas used in the management of CMPA

- No known food or drug allergy
- No impairment in taste or smell perception
- Not experiencing an acute upper respiratory tract infection at the time of evaluation
- No participation in any formula taste-testing study related to CMPA within the past 3 months.

Testing was conducted on seven substitution formulas without added sweeteners or additional flavorings available on the market: Two AAFs (Neocate-Numil<sup>®</sup>, Alfamino-Nestlé<sup>®</sup>), one AAF with synbiotics (Pregomin Syneo-Numil<sup>®</sup>), one AAF specifically designed to meet the nutritional and lifestyle needs of children over 1 year of age (Neocate Junior-Numil<sup>®</sup>), one synbiotic eHF (Aptamil Pepti Syneo-Numil<sup>®</sup>), and two rice protein-based formulas (Evolvia RP1-Montero<sup>®</sup> and Evolvia RP2-Montero<sup>®</sup>). A sensory evaluation was conducted using a single-blind protocol, following the methodology previously applied in the CONTEST-1 study.<sup>6</sup> In brief, each formula was assigned a randomly generated three-digit code and was presented without branding or packaging. Test samples were prepared in equal volumes (30 mL) and served sequentially. All formula preparations were carried out in a separate area to minimize visual or contextual bias. Water and plain crackers were provided as palate cleansers before each tasting. The entire evaluation procedure was completed in approximately 10 min per participant. After tasting all the samples, participants completed a structured questionnaire evaluating each formula's taste, smell, and appearance. They also provided feedback on the suitability of each product for children diagnosed with CMPA. Sensory attributes were rated on a numerical scale from 0 (least liked) to 10 (most liked). Additionally, participants were asked to indicate the most and least preferred characteristic (taste, smell, or appearance) for each formula.

Ethical approval for this study was obtained from the Non-Invasive Clinical Research Ethics Committee of Eskişehir Osmangazi University Faculty of Medicine (2023/27). All participants provided written informed consent before participation, in accordance with the Declaration of Helsinki.

## Statistics

Descriptive statistics (mean, standard deviation, median, minimum, and maximum) were used to summarize continuous variables. Categorical variables were presented as frequencies and percentages. The normality of distribution was assessed using the Shapiro-Wilk test. For comparisons between two independent non-normally distributed continuous variables, the Mann-Whitney U test was applied. The Wilcoxon Signed-Rank test was used to compare two related non-normally distributed continuous variables. Associations between categorical variables were analyzed using the Chi-square test. A P-value of < 0.05 was considered statistically significant. All analyses were performed using MedCalc Statistical Software version 12.7.7 (MedCalc Software bvba, Ostend, Belgium; <http://www.medcalc.org>; 2013).

## Results

Neocate Junior-Numil<sup>®</sup> was the most preferred product based on taste scores among mothers and physicians. The top three rankings are presented in Table 1.

As shown in Table 1, according to the evaluations of mothers, the most preferred product in terms of taste was Neocate Junior-Numil<sup>®</sup> with 49.6%, followed by Aptamil Pepti Syneo-Numil<sup>®</sup> and Evolvia RP2-Montero<sup>®</sup> at 32.8 and 23.4%, respectively. Similarly, based on the evaluations by physicians, Neocate Junior-Numil<sup>®</sup> ranked first with 62.4%, followed by Aptamil Pepti Syneo-Numil<sup>®</sup> and Alfamino-Nestlé<sup>®</sup> at 42 and 22.1% of preference, respectively.

In terms of smell preference, Neocate Junior-Numil<sup>®</sup> received the highest mean scores from both mothers and physicians, followed by Aptamil Pepti Syneo-Numil<sup>®</sup>. Moreover, mothers rated the smell of both Neocate Junior-Numil<sup>®</sup> and Aptamil Pepti Syneo-Numil<sup>®</sup> significantly higher than physicians did ( $P < 0.001$  and  $P = 0.005$ , respectively). For all other formulas, no statistically significant differences were found between mothers and physicians regarding smell preference scores (Table 2).

**Table 1** Taste-based rankings of formulas by mothers and physicians.

Name of formula	Mothers' ranking			Physicians' ranking		
	First line n (%)	Second line n (%)	Third line n (%)	First line n (%)	Second line n (%)	Third line n (%)
Neocate Junior <sup>®</sup>	68 (49.6)	29 (21.2)	14 (10.2)	113(62.4)	32 (17.7)	11 (6.1)
Aptamil Pepti Syneo <sup>®</sup>	39 (28.5)	45 (32.8)	26 (19)	43 (23.8)	76 (42)	34 (18.8)
Evolvia RP2 <sup>®</sup>	10 (7.3)	16 (11.7)	32 (23.4)	6 (3.3)	17 (9.4)	38 (21)
Alfamino <sup>®</sup>	8 (5.8)	19 (13.9)	27 (19.7)	8 (4.4)	20 (11)	40 (22.1)
Evolvia RP1 <sup>®</sup>	7 (5.1)	7 (5.1)	15 (10.9)	2 (1.1)	6 (3.3)	19 (10.5)
Neocate <sup>®</sup>	3 (2.2)	9 (6.6)	11 (8)	3 (1.7)	12 (6.6)	16 (8.8)
Pregomin Syneo <sup>®</sup>	2 (1.5)	12 (8.8)	12 (8.8)	6 (3.3)	18 (9.9)	23 (12.7)
Total	137	137	137	181	181	181

Data are presented as n (%). Mothers n = 137, Physicians n = 181.

Percentages are calculated within each group and may not add up to 100% due to multiple rankings.

**Table 2** Evaluation of perceived smell scores of formulas by participant group.

	Mothers' ranking		Physicians' ranking		P
	Mean ± SD*	Median (min-max)	Mean ± SD*	Median (min-max)	
Neocate Junior®	(6.8 ± 2.5)	7 (1-10)	(5.8 ± 2.4)	6 (1-10)	<b>&lt;0.001</b>
Aptamil Pepti Syneo®	(6.1 ± 2.6)	6 (1-10)	(5.4 ± 2.3)	5 (1-10)	<b>0.005</b>
Alfamino®	(4.4 ± 2.6)	4.5 (1-10)	(4.2 ± 2.3)	4 (1-9)	0.475
Evolvia RP2®	(4.4 ± 2.7)	4.5 (1-10)	(3.9 ± 2.3)	3 (1-10)	0.176
Pregomin Syneo®	(3.6 ± 2.5)	3 (1-10)	(3.5 ± 2.1)	3 (1-10)	0.881
Neocate®	(3.4 ± 2.4)	3 (1-10)	(3.3 ± 2.2)	3 (1-10)	0.859
Evolvia RP1®	(3.4 ± 2.5)	2.5 (1-10)	(2.9 ± 2.1)	2 (1-10)	0.302

\*SD: Standard deviation, data are presented as mean ± SD and median (min-max).

1: I do not like at all; 10: I definitely like very much.

**Table 3** Assessment of appearance scores of formulas by mothers and physicians.

	Mothers' ranking		Physicians' ranking		P
	Mean ± SD*	Median (min-max)	Mean ± SD*	Median (min-max)	
Neocate Junior®	(7.2 ± 2.3)	8 (1-10)	(6.9 ± 2)	7 (1-10)	0.182
Neocate®	(6.1 ± 2.7)	6 (1-10)	(6.7 ± 2.1)	7 (1-10)	<b>0.039</b>
Aptamil Pepti Syneo®	(6.7 ± 2.4)	7 (1-10)	(6.6 ± 2)	7 (2-10)	0.355
Pregomin Syneo®	(6.1 ± 2.7)	6 (1-10)	(6.5 ± 2.1)	7 (1-10)	0.191
Alfamino®	(5.4 ± 2.5)	6 (1-10)	(5.3 ± 2.2)	6 (1-10)	0.630
Evolvia RP1®	(3.9 ± 2.6)	3 (1-10)	(3.9 ± 2.2)	3.5 (1-10)	0.640
Evolvia RP2®	(4.3 ± 2.8)	4 (1-10)	(3.8 ± 2.2)	3.5 (1-10)	0.413

\*SD: Standard deviation, data are presented as mean ± SD and median (min-max).

1: I do not like at all; 10: I definitely like very much.

**Table 4** Comparison of sensory perception scores of formulas between mothers and physicians.

	Mothers' ranking		Physicians' ranking		P
	Mean ± SD*	Median (min-max)	Mean ± SD*	Median (min-max)	
Neocate Junior®	(6.8 ± 2.4)	7 (1-10)	(6.4 ± 2)	7 (1-10)	<b>0.023</b>
Aptamil Pepti Syneo®	(6.5 ± 2.3)	7 (1-10)	(5.6 ± 2)	6 (1-10)	<b>&lt;0.001</b>
Evolvia RP2®	(4.4 ± 2.5)	4 (1-10)	(3.7 ± 2)	3 (1-10)	<b>0.022</b>
Alfamino®	(4.3 ± 2.5)	4 (1-10)	(4 ± 2)	4 (1-9)	0.259
Neocate®	(3.6 ± 2.3)	3 (1-10)	(3.4 ± 1.8)	3 (1-8)	0.756
Pregomin Syneo®	(3.6 ± 2.2)	3 (1-10)	(3.7 ± 2)	3 (1-9)	0.414
Evolvia RP1®	(3.5 ± 2.5)	3 (1-10)	(3 ± 1.9)	3 (1-9)	0.314

\*SD: Standard deviation, data are presented as mean ± SD and median (min-max).

1: I do not like at all; 10: I definitely like very much.

When evaluated in terms of product appearance, Neocate Junior-Numil® received the highest appearance scores from both mothers and physicians. Additionally, physicians rated the appearance of Neocate-Numil® significantly higher than mothers did (P = 0.039). No

statistically significant differences were observed between the two groups for any of the other formulas with respect to appearance scores (Table 3).

A combined evaluation of taste, smell, and appearance revealed that parental scores for Neocate Junior-Numil®,

**Table 5** Physician ratings of formula suitability in CMPA.

Physicians	Mean $\pm$ SD*	Median (min-max)
Neocate®	(3.5 $\pm$ 2.1)	3 (1-10)
Neocate Junior®	(6.5 $\pm$ 2.3)	7 (1-10)
Pregomin Syneo®	(3.8 $\pm$ 2.1)	4 (1-10)
Aptamil Pepti Syneo®	(5.9 $\pm$ 2.4)	6 (1-10)
Evolvia RP1®	(3.1 $\pm$ 2.1)	3 (1-9)
Evolvia RP2®	(4 $\pm$ 2.3)	4 (1-10)
Alfamino®	(4.2 $\pm$ 2.2)	4 (1-10)

\*SD: Standard deviation.

1: I do not like at all; 10: I definitely like very much.

Aptamil Pepti Syneo-Numil®, and Evolvia RP2-Montero® were significantly higher than those of physicians ( $P = 0.023$ ,  $P < 0.001$ , and  $P = 0.022$ , respectively) (Table 4).

Table 5 presents the products that physicians considered most appropriate for children diagnosed with CMPA. Accordingly, the product deemed most appropriate by physicians was Neocate Junior-Numil® with a mean score of  $6.5 \pm 2.3$ , followed by Aptamil Pepti Syneo-Numil® ( $5.9 \pm 2.4$ ) and Alfamino-Nestle® ( $4.2 \pm 2.2$ ).

Tables 6 and 7 present a comparative analysis of the most liked and least preferred attributes of the formulas as evaluated by mothers and physicians.

While 18.7% of physicians ( $n = 34$ ) reported having previously tasted any of the medical formulas developed for children with CMPA, 68.8% of mothers ( $n = 95$ ) stated that they had done so.

## Discussion

In our study, the most preferred product in terms of taste, smell, and appearance by both mothers and physicians was an AAF specifically developed to meet the increasing nutritional requirements of children over 1 year of age. The favorable palatability of a formula plays a critical role in product acceptance, which in turn contributes to symptom improvement and positively influences growth and development. In this study, taste was identified by both mothers and physicians as the most decisive factor influencing formula selection among the characteristics that define palatability. Several studies in the literature suggest that infants exhibit taste response patterns similar to those of adults, particularly in reaction to sweet and bitter stimuli, due to their early exposure to amniotic fluid, breast milk, and solid foods.<sup>4,9</sup> Ideally, palatability assessments should be conducted directly with infants themselves. Assessing taste perception in infants presents methodological challenges. In this context, the sensory evaluations made by caregivers—particularly mothers—based on their own perceptions become significant for two main reasons. First, it is well established that maternal dietary patterns during pregnancy can shape the infant's early exposure to flavors.<sup>10</sup> Second, mothers tend to perceive formulas they personally find palatable as more suitable for their infants, which may indirectly influence the infant's acceptance of

**Table 6** Distribution of most liked sensory attributes across formulas.

	Mothers n (%)	Physicians n (%)	P
Neocate®			
Appearance	62 (47)	109 (67.7)	<b>0.0004</b>
Smell	10 (7.6)	7 (4.3)	0.229
Taste	9 (6.8)	6 (3.7)	0.244
Neocate Junior®			
Appearance	17 (14.4)	25 (17.9)	0.4492
Smell	16 (13.6)	15 (10.7)	0.4764
Taste	68 (57.6)	85 (60.7)	0.6143
Pregomin Syneo®			
Appearance	58 (45)	101 (61.6)	<b>0.0047</b>
Smell	7 (5.4)	5 (3)	0.3021
Taste	17 (13.2)	15 (9.1)	0.2645
Aptamil Pepti Syneo®			
Appearance	23 (19.5)	31 (21.4)	0.7050
Smell	19 (16.1)	16 (11)	0.2265
Taste	65 (55.1)	76 (52.4)	0.6629
Evolvia RP1®			
Appearance	20 (15.3)	29 (16.8)	0.7253
Smell	12 (9.2)	15 (8.7)	0.8798
Taste	23 (17.6)	15 (8.7)	<b>0.0205</b>
Evolvia RP2®			
Appearance	16 (12.7)	24 (14.8)	0.6097
Smell	16 (12.7)	36 (22.2)	<b>0.0379</b>
Taste	32 (25.4)	24 (14.8)	<b>0.0244</b>
Alfamino®			
Appearance	34 (27.2)	55 (34.8)	0.1722
Smell	18 (14.4)	21 (13.3)	0.7902
Taste	23 (18.4)	30 (19)	0.898

the product.<sup>11</sup> Mothers and physicians were included in the study group, given the critical role of their perspectives in evaluating formula acceptability.

The initial report on the palatability of formulas used in children with CMPA was published.<sup>3</sup> In this study, 50 adults were asked to evaluate 12 different formulas—nonhydrolyzed, partially hydrolyzed, casein-based, whey-based hydrolysates, soy-based formulas, and rice-based hydrolysates—based on their taste, smell, and texture. The highest taste scores were given to soy- and rice-based formulas, while palatability—particularly in terms of taste—declined as the degree of hydrolysis increased. However, AAFs were not included in this study. A study conducted in the Netherlands in 2014 was the first to compare the palatability of an amino acid-based formula and an eHF.<sup>7</sup> In this study, eHFs were categorized into two groups based on their protein source: whey and casein hydrolysates. The palatability evaluation was performed using three different formulas—whey-based eHF, casein-based eHF, and an AAF—with the participation of 40 physicians. The findings indicated that the taste score of the AAF fell between those of the two eHFs, partially confirming the results reported by Pedrosa et al.<sup>3</sup> Subsequent studies have also demonstrated that while whey-based eHFs tend to have a more

**Table 7** Most disliked product attributes (taste, smell, appearance) reported by mothers and physicians.

	Mothers n (%)	Physicians n (%)	P
<b>Neocate®</b>			
Appearance	3 (2.6)	2 (1.3)	0.4364
Smell	13 (11.1)	15 (9.9)	0.7503
Taste	91 (77.8)	118 (78.1)	0.9532
<b>Neocate Junior®</b>			
Appearance	4 (3)	4 (2.4)	0.7498
Smell	12 (9.1)	32 (19.3)	<b>0.0139</b>
Taste	36 (27.3)	33 (19.9)	0.1333
<b>Pregomin Syneo®</b>			
Appearance	4 (3.3)	3 (2)	0.5022
Smell	13 (10.8)	25 (16.4)	0.1862
Taste	85 (70.8)	104 (68.4)	0.6702
<b>Aptamil Pepti Syneo®</b>			
Appearance	6 (4.5)	12 (7.2)	0.3289
Smell	17 (12.8)	37 (22.2)	<b>0.0357</b>
Taste	28 (21.1)	40 (24)	0.5521
<b>Evolvia RP1®</b>			
Appearance	19 (16.1)	15 (10.6)	0.1915
Smell	16 (13.6)	27 (19)	0.2443
Taste	74 (62.7)	88 (62)	0.9079
<b>Evolvia RP2®</b>			
Appearance	31 (25)	31 (21.2)	0.4601
Smell	8 (6.5)	22 (15.1)	<b>0.0255</b>
Taste	69 (55.6)	77 (52.7)	0.6344
<b>Alfamino®</b>			
Appearance	9 (7.2)	15 (9.5)	0.4912
Smell	17 (13.6)	23 (14.6)	0.8109
Taste	73 (58.4)	92 (58.2)	0.9730

favorable taste profile, there is substantial variation in palatability even among different eHFs.<sup>4,5</sup> Miraglia et al.<sup>4</sup> associated differences in palatability, despite identical degrees of hydrolysis, with variations in saturated fatty acid and lactose content. In their randomized, double-blind, multicenter study involving 150 adult participants, they demonstrated that increasing levels of saturated fat and lactose were linked to improved palatability. Similarly, a study conducted in the United Kingdom involving 100 adults evaluated four different eHFs used in CMPA management and reported that the two lactose-containing formulas received the highest taste scores.<sup>5</sup>

In the CONTEST-1 study published in 2022, consistent with the findings of our study, the formula that received the highest scores in terms of taste, smell, and appearance was an AAF specifically designed for children over 1 year of age.<sup>6</sup> Although the relationship between product composition and taste perception was not examined due to methodological constraints, the same formula was identified as the first choice by both mothers and physicians in two independent studies conducted at different centers using different formula types. Studies on taste perception in adults have shown that it can vary significantly depending on multiple factors, including genetics, age, sex, and

cultural background.<sup>12-14</sup> A study comparing taste thresholds in Thai adults, who typically consume diets rich in spices, and Japanese individuals found that Thai participants exhibited lower taste sensitivity than their Japanese counterparts.<sup>12</sup> These findings suggest that dietary culture may also play a significant role in shaping taste perception. In another study conducted in adults, Aoki et al.<sup>13</sup> reported that genotypic variations may influence taste receptor gene expression and affect sensitivity to bitter tastes.

Research on taste in children traces back to the fetal period. It has been reported that, particularly during the last trimester of pregnancy, the development of the gustatory and olfactory systems enables the fetus to perceive environmental stimuli. For this reason, the fetus may respond to taste components present in the amniotic fluid, which vary depending on the maternal diet, either through swallowing or pseudorespiration.<sup>15-17</sup> These prenatal sensory experiences play an important role in shaping the foundations of postnatal feeding behaviors. The commonly observed postnatal aversion to sour and bitter tastes in many children has been explained by two factors. The first is thought to be an evolved, innate survival mechanism. The second may be related to variations in the TAS2R38 gene, which encodes receptors potentially involved in bitter taste perception. These genetic variations are believed to influence individual taste sensitivity and may contribute to interindividual differences.<sup>18,19</sup> In conclusion, both maternal diet and genetic factors may reduce a newborn's opportunity to become familiar with certain taste profiles.

The bitter taste of hypoallergenic formulas is known to cause difficulties in the management of CMPA. Studies have shown that these formulas are better tolerated when introduced before 4 months of age, whereas older infants are more likely to reject them.<sup>4,20-23</sup> Palatability becomes particularly important in infants over 6 months of age or in those who have experienced multiple formula changes. As these infants have already encountered a variety of flavors, they tend to become more selective in their taste preferences.<sup>8</sup>

This study demonstrated that an unflavored formula was also acceptable to older children with a more developed sense of taste. The fact that this product was processed using a different technology specifically for children over 1 year of age may have reduced the impact of bitterness-inducing compounds. As also noted in the CONTEST 1 study, technological processing methods may help achieve this outcome by lowering fatty acid oxidation and increasing the proportion of neutral-tasting components.<sup>6</sup>

In the present study, both mothers and physicians ranked taste as the most important factor in palatability, followed by smell and appearance. Based on these three characteristics, physicians were asked to indicate the most appropriate formula options for infants diagnosed with CMPA. The three formulas that received the highest taste scores from physicians also ranked among the top three most appropriate options. Although there is no direct data linking physicians' taste perceptions to infants' acceptance of formulas, some studies suggest that physician preferences may be associated with patient attitudes.<sup>24</sup> Therefore, a pediatrician's product preference may exert an indirect yet meaningful influence on both the

acceptance of the formula and its integration into clinical practice.

Formula acceptance in infants with CMPA is important not only for symptom resolution but also in terms of healthcare expenditures. It is well known that healthcare costs are likely to be higher in CMPA cases requiring multiple formula changes. Although our study was not designed as a cost-effectiveness analysis, we believe that selecting a formula with adequate palatability may help prevent unnecessary healthcare spending.

In the present study, two synbiotic-containing formulas were included: one AAF and one eHF, neither of which had been featured in previous research. According to the current literature, the addition of certain probiotics to hypoallergenic formulas may enhance the development of tolerance in infants with CMPA. Some evidence also suggests a potential benefit in reducing the risk of severe wheezing in these infants. However, in cases of non-IgE-mediated CMPA, such effects on tolerance development and wheezing have not been observed. Nevertheless, this is supported by evidence with low to very low certainty.<sup>25</sup> To date, no studies in the literature have directly compared the palatability of synbiotic-enriched hypoallergenic formulas with that of other hypoallergenic formulas.

The primary limitation of our study is that it was conducted in adult participants. A second important limitation is its cross-sectional design. Acceptance levels and user experiences that may change over time were not assessed. Therefore, prospective studies are needed to investigate the long-term relationship between formula palatability, acceptance, and symptom control.

## Conclusion

The selection of an appropriate formula plays a critical role in the management of CMPA by ensuring symptom resolution, supporting growth and development, and improving the quality of life of children. In the long term, children with CMPA may experience changes in eating behaviors and food preferences. Therefore, choosing formulas with acceptable palatability is important not only for achieving short-term treatment success but also for preventing the development of selective eating behaviors and promoting healthy dietary habits.

## Author's Contributions

All authors contributed equally to this article.

## Conflict of Interest

The authors declare no potential conflicts of interest with respect to the authorship and/or publication of this article.

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