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SENSORY ANALYSIS OF LIQUID ORAL DOSAGE FORMS ANTACID SUSPENSIONS

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ABSTRACT

Sensory analysis of pharmaceutical oral dosage forms can be used effectively in product development and quality control to improve patient acceptance of the drug. In this work, sensory analysis is applied to detect consumer preference for formulations of aluminum and magnesium hydroxide antacid suspensions.

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A ranking test was applied to six peppermint flavored commercial samples (identified from A to F) of the antacid with the same therapeutical potency. The samples corresponded to four different formulations and six batches from three manufacturers. The ranking test was applied in duplicate to ten judges (ages 20-34) trained in the method and in the main sensory characteristics of the product. The coded samples were presented randomly in duplicate to each judge with six replications, and results were recorded in a preference scale from 1 to 6 (1 = most preferred). Statistical analysis of the data considered the sample as the only cause for variation and the minimum significant difference was determined at confidence levels of $\alpha = 0.01$ and $\alpha = 0.05$. The results show a highly significant preference ($\alpha = 0.01$) in sample F over A, B, D and E. At $\alpha = 0.05$, sample F was preferred over all the others, whereas formulations A and D were the least preferred at both significance levels. These results demonstrate that sensory analysis can be applied succesfully in product selection for the patient, formulation development and as a quality control tool in antacid suspensions.

INTRODUCTION

Sensory quality can be understood as an integration of specific attributes detected by the consumer through her (his) senses. Aside of the therapeutical value of the drug, the sensory attributes are of direct importance in some oral dosage forms (suspensions, syrups, chewable tablets) in the decision by the patient to comply with the therapy. The main objective in considering product

development and quality control through sensory evaluation of the drug is to maintain the treatment by the patient.

Sensory analysis is a relatively new scientific discipline that has been defined by the Sensory Evaluation Division of the Institute of Food Technologists (IFT) in the United States as "A scientific discipline that calls for, measures, analyses and interprets the reactions as they are detected by the olfactory, visual, auditory and tactile senses", cited by Iturbe and Valdivia (1).

Research on the organoleptic properties of foods reached a climax in 1937 when the American Chemical Society organized a symposium on this topic. The interest on acceptability studies of foods intensified during World War II when hundreds of hungry soldiers rejected their highly nutritious foods because of the poor sensory attributes of the rations. Since 1970, several universities throughout the world have included in their academic programs the study of sensory evaluation in food related curricula (1).

In relation to the application of sensory analysis in pharmaceutical oral dosage forms, we only found one report on the application of this tool in an on-line literature search conducted through the International Pharmaceutical Abstracts and covering from 1980 to 1992 (2). The keywords used were "sensory analysis" and "sensory analysis, finished product". The study (3) was a double-blind, crossover trial to detect preference in 100 healthy volunteers (aged 22-65 years) for formulations of cholestyramine powder with either sucrose or aspartame and with chilled water and orange juice. The judges preferred (statistically significant) a formulation that

contained aspartame as sweetener. The importance of organoleptic properties in product development and quality control of pharmaceutical oral dosage forms is discussed in more detail in standard reference books (4-7).

The methods used by sensory analysis can be classified in: 1) objective evaluation methods and 2) subjective evaluation methods. The latter is based in an evaluation carried out by a team of judges that can or cannot be trained in the method and in the characteristics of the product. These methods can be used in product development, process changes, formulation changes, quality control and stability testing (1).

For many years, antacids have been used effectively in the treatment of gastrointestinal conditions. It has been reported that intensive antacid treatments are effective in healing gastric ulcers (8-12). Further, in one report (8) it is stated that antacids combined with cimetidine or ranitidine have a synergistic effect in healing peptic ulcers with healing rates close to 100%.

From the standpoint of organoleptic characteristics, it has been recognized that certain flavors become monotonous if they have to be taken daily, and sometimes several times a day, for extended periods of time, as would be the case for an intensive antacid therapy. It is thought that less exotic flavors, such as peppermint, might be best for these kinds of products (5).

In an study on the evaluation of aluminum hydroxide and magnesium hydroxide antacid suspensions, Hem and coworkers (13) stated that an antacid suspension cannot be adequately evaluated by a single

test and established four criteria to assist in product selection. In another report, Jiménez Torres, Peidró Martínez and Mut Aguilar (14) used these criteria as indication of the quality of antacid suspensions. The four criteria are (13):

1. The volume of antacid required to neutralize 40 meq of acid should be less than 15 ml.
2. The antacid should contribute less than 10% (50 mg) of the daily sodium allowed in a strict sodium-restricted diet when used in a regimen of seven doses per day each capable of neutralizing 40 meq of acid.
3. At least 90% of the antacid should react within 15 minutes at pH 3 and 37°C.
4. The content uniformity, measured as the combined coefficient of variation for equivalent aluminum oxide and magnesium hydroxide, should be less than 10%.

In another study, Peidró Martínez and Jiménez Torres (15) indicated that, in the evaluation of this type of antacids, flavor has to be considered as well as the physicochemical characteristics.

We believe that organoleptic properties, such as color, odor, flavor and settled solids ratio would have to be considered also as indicators of the quality of the drug and taken into account by the physician to select the right prescription for the patient being treated, since they would improve patient compliance with the therapy. The organoleptic characteristics of aluminum hydroxicarbonate and magnesium hydroxide antacid suspensions can be optimized to improve patient acceptance of the drug. Further, sensory evaluation can be applied to commercial products in the market to identify the

preferred formulation for a given group of patients according to age.

The objective of this work is to demonstrate the applicability of sensory analysis in pharmaceutical oral dosage forms using liquid antacids as a test product to determine consumer preference in six commercial samples of aluminum hydroxicarbonate and magnesium hydroxide suspensions, peppermint flavored and with the same therapeutical potency.

MATERIALS AND METHODS

The commercial samples studied were acquired in a local drugstore and with a local manufacturer. The samples were used as received and were identified as A, B, C, D, E and F and classified regarding formulation type, manufacturer and batch according to Table 1.

A randomized complete block design was used in this study to determine preference of the six samples with each day in which tests were performed corresponding to one block. Each block consisted in presenting six different samples in duplicate to each of ten judges (ages 20-34) trained in the method and in the sensory characteristics of the product. The judges were selected from a group of 16 candidates (ages 18-34). Selective tests consisted in threshold determination in three flavors: sweet, salty and peppermint (the flavor of the antacid formulations). The aqueous solutions used were sucrose (2, 1, 0.5, 0.25 and 0.125%, w/v), sodium chloride (0.4, 0.2, 0.1, 0.05 and 0.025%, w/v) and a commercial peppermint essence (McCormik & Co., Inc., Baltimore) prepared using 10 ml of the flavor, 20 g of sucrose, bringing

TABLE 1

Classification of samples regarding formulation, manufacturer and batch

SAMPLE	FORMULATION	MANUFACTURER	BATCH
A	a	1	w
B	b	2	x
C	c	1	y
D	a	1	u
E	d	3	z
F	c	1	v

the volume to one liter with water and making dilutions from this stock solution (1:2, 1:4, 1:8, 1:16 and plain water). The volume of sample used in these tests was 50 ml. The judges were instructed to report the coded sample in which they detected the threshold concentration of each flavor. Results of this test were linearly correlated as percent of candidates that detected the flavor versus flavor concentration.

Triangular tests (16) were used to determine the ability of the candidates to detect differences between samples of the antacid formulations. To this end, a sample of formulation D was used as such and with the addition of 5 g/L of sucrose . Combinations of these two formulations were presented to the candidates (10 ml samples) and they were asked to report the one that was different from the other two. A similar test was carried out with unaltered samples of formulation D, from two batches manufactured with a difference of one year. Results of this test were

analyzed to detect significant differences using the χ^2 distribution.

In the ranking tests (17), judges were instructed to test all samples and then to write down his (her) preference assigning number 1 to the most preferred sample, number 2 to the second in preference and so on up to number 6 for the least preferred sample. Additionally, the judges were asked to write down any observations in relation to other sensory characteristics of the samples, such as sweetness, sourness, saltiness, etc.

Ranking tests were analyzed following the multiple comparison methods reported by Joanes (17) and also by a one-way analysis of variance of absolute differences between the sums of ranks with respect to the day of the test, and considering the samples as the only cause of variation.

In all tests, judges were instructed not to swallow the sample and to rinse their mouths with potable water after testing each sample.

RESULTS AND DISCUSSION

A group of 10 judges were selected from the original 16 candidates. Although all candidates detected the flavors tested and were able to determine differences between samples, criteria for selecting the 10 finalists were interest in the experiment and punctuality to attend the selective and training sessions.

The threshold concentration detected by 50% of the candidates was 4.15 g/L for sucrose, 1.02 g/L for NaCl and 3.08 ml of essence/L for peppermint. Thresholds for basic flavors and others are reported in the literature, and they are not always directly

comparable because of different factors (techniques, chemicals, inadequate number of tests, etc.), however for sucrose and salt we found values of 5.4 g/L and 0.71 g/L for sucrose and sodium chloride respectively (16). We found no value reported for peppermint.

Data obtained from the ranking test can be observed in Table 2 as sums of ranks per sample, per day. The lowest value corresponds to the most preferred sample, and the highest to the least preferred sample. So, according to Table 2, sample F is preferred over all the others.

Table 3 reports the results obtained from the one-way analysis of variance, where samples are considered as the only cause of variation. According to Table 3, there is a highly significant difference ($\alpha = 0.01$) between samples. We applied a minimum significant difference test between each pair of samples to determine significant preference at two confidence levels (0.05 and 0.01). Results are indicated in Table 4.

A highly significant difference ($\alpha = 0.01$) can be observed in sample F (preferred) versus samples A, D, B, and E, as well as sample C (preferred) versus samples A, D, and B; and samples E and B (preferred) versus samples A and D. Significant difference ($\alpha = 0.05$) can be observed in sample F (preferred) versus sample C, sample C (preferred) versus sample E, and sample E (preferred) versus sample B. No significant difference ($\alpha = 0.05$) can be observed between samples A and D.

If we relate preference with sample formulation, Table 4 shows that all formulations are significantly different from each other ($\alpha = 0.05$). It can be stated, too, that there is a significant difference between samples F and C: same formulation, but

TABLE 2

Ranking test for preference: Sums of ranks per sample, per day

SAMPLE	DAY						SUM	AVERAGE	S.D.
	1	2	3	4	5	6			
A	98	96	101	99	94	100	588	98.00	2.61
B	95	65	73	65	76	69	443	73.83	11.25
C	46	59	52	56	51	56	320	53.33	4.63
D	81	88	95	103	87	80	534	89.00	8.74
E	54	71	70	65	61	64	385	64.17	6.24
F	46	41	29	32	51	51	250	41.67	9.46

S.D. = Standard deviation

TABLE 3

Analysis of variance. Sum of ranks of samples per day

CAUSE OF VARIATION	DEGREES OF FREEDOM	SUM OF SQUARES	MEAN SQUARES	F
Sample	5	13,646	2,729	45.53**
Error	30	1,798	60	
Total	35	15,444		

**Exists significant differences between samples.

different batches; although this is not observed between samples A and D which present the same situation.

All judges agreed that sweetness is a more relevant factor of preference than acidity. Most of them preferred a sample not too sweet, except a few of them who preferred the sweetest one. Sweetness is a

TABLE 4

Correlations between each pair of samples. Minimum significant differences between averages at 5% (*) and 1% (**).

SAMPLES (AVERAGE)	A (98.00)	D (89.00)	B (73.83)	E (64.17)	C (53.33)	F (41.67)
F(41.67)	56.33**	47.33**	32.16**	22.50**	11.66*	0.00^{NS}
C(53.33)	44.67**	35.67**	20.50**	10.84*	0.00^{NS}	
E(64.17)	33.83**	24.83**	9.66*	0.00^{NS}		
B(73.83)	24.17**	15.17**	0.00^{NS}			
D(89.00)	9.00^{NS}	0.00^{NS}				
A(98.00)	0.00^{NS}					

NS = No significance at 5% confidence level.

subjective perception of judges, since we did not quantitatively determined it, data on sweetness do not have satistical value, they only provide an idea of some relevant factors related with preference since they come from observations made by trained judges and this factor should be considered in formulation development for antacid suspensions.

CONCLUSIONS

From the data obtained , it is possible to determine significant difference in preference of samples with different formulation, as can be observed in sample F versus samples A, D, B and E. This result can be used as a tool in development of successful oral antacid formulations improving patient's compliance

with the therapy. It is possible too, to determine significant difference in preference between samples with the same formulation, which proceed from different batches, as in samples F and C; this determination can be used as a quality control tool to confirm homogeneity in sensorial attributes between batches. The methodology reported here for antacid aluminum and magnesium hydroxide formulations could be applied to other oral liquid dosage forms, such as syrups. Ongoing work to determine flavor preference for product development and batch to batch variation as a qualitiy control tool will be reported in forthcoming publications.

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