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ORIGINAL ARTICLE

Diclofenac fast-dissolving film: suppression of bitterness by a taste-sensing system

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Abstract

Context: The selection of a proper taste-masking agent (TMA) is a critical issue in the development of fast-dissolving films containing bitter drugs. *Objective*: This work is aimed to evaluate the suppression of the bitter taste of a maltodextrin fast-dissolving film loaded with 13.4 mg sodium diclofenac (DS) by adding TMAs. *Methods*: The films were prepared by casting and drying aqueous mixtures of maltodextrin (DE = 6), glycerin, sorbitan oleate, and DS. Films were characterized in terms of thickness, tensile properties, film disintegration time, and drug dissolution time. The bitterness intensity of DS and the masking effect of TMAs were evaluated by an electronic tongue. *Results*: The 'mint' and 'licorice' flavors and sucralose mixture resulted appropriate to mask DS bitterness as confirmed by a panel of volunteers. The addition of these TMAs did not significantly affect the film disintegration time (15–20 seconds) and DS dissolution rate (about 5 minutes). *Conclusion*: The electronic tongue was allowed to discriminate the effect of the TMA also in the presence of other hydrosoluble constituents of the film. Therefore, because of its simplicity and rapidity, this technique could assist or even replace the sensory evaluation in the development of fast-dissolving films.

Key words: Bitter drug, electronic tongue, maltodextrin, taste-masking agent, tensile properties

Introduction

Fast-dissolving oral delivery systems are solid dosage forms that disintegrate or dissolve rapidly (<1 minute) when placed in the mouth, without drinking or chewing[1]. Among the variety of polymers available as film-forming materials, maltodextrins (MDX) plasticized by glycerin have been recently proposed to produce fast-dissolving films by solvent casting and hot-melt extrusion[2].

In the development of orodispersible films, the main critical issues are represented by the tensile properties required for packaging and handling procedures, dissolution in the oral cavity, stability, and taste. Generally speaking, organoleptic characteristics are important parameters that drive patients' acceptance and compliance, and taste is one of the prime factors determining the market penetration and commercial success of oral pharmaceuticals. The development of more desirable and palatable formulations often represents a challenge for pharmaceutical companies, which are currently investing time and cost in the study of taste-masking techniques. Indeed, palatability differs greatly among individuals and is affected by compatibility between drugs and additives and no universally applicable technology for taste-masking reduction has ever been recognized. Flavors, sweeteners, and amino acids can reduce or suppress the perception of bitterness of several pharmaceuticals and are generally used in association with other taste-masking techniques[1]. An alternative approach is the addition of complexing agents, such as β-cylodextrin[3]. Other technologies are based on coating with polymers that could delay or moderate dissolution, microencapsulation, ion-exchange resins, and conventional granulation[4].

To evaluate the taste-masking efficiency during pharmaceutical formulation development, in vivo or in vitro methods have been proposed[5]. The in vivo studies included human panel test, electrophysiological methods,

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and animal preference tests. Human taste panel study consists of evaluating the samples by estimating the gustatory sensation responses in healthy human volunteers within well-controlled procedures. The in vitro approaches for taste assessment are drug release studies and in vitro assays. The former is an indirect method which does not contribute to the evaluation of the drug product taste and it is commonly used to measure the effectiveness of coating and/or complexation.

The taste masking of such dosage form is particularly critical because, compared to the conventional liquid dosage forms, active ingredient is not diluted and the taste-masking agent (TMA) loading is limited with respect to orodispersible tablets because of the low weight of the film. Recently, the electronic tongue (ET) has become a useful tool to taste-active compounds in taste measurement technology because of its simplicity, speed, relatively low cost, and lack of risk[6–9]. The ET is a liquid analytical device composed of an array of weakly specific chemical sensors combined with a pattern recognition system. The aim of this work was to study a palatable MDX fast-dissolving films containing sodium diclofenac (DS), selected as a model of bitter drugs. TMAs, namely, sweeteners and flavors, were selected using an ET. Moreover, considering that TMAs could compromise the film mechanical properties, disintegration time, and drug dissolution rate, their effects were also investigated.

Materials and methods

Materials

MDX having a DE equal to 6 (Glucidex® IT6, MDX6) was obtained by Roquette (Lestrem, France). DS, sorbitan oleate (SO), glycerol (GLY), sucralose, saccharine, and xylitol were purchased from Farmalabor (Canosa di Puglia, Bari, Italy). Mint, licorice, and soft fruits flavors were kindly provided by Kerry Ingredients & Flavours Italia (Mozza, Bergamo, Italy). All solvents were of analytical grade, unless specified.

Film preparation

The aqueous dispersion of MDX6, GLY, and SO in distilled water was prepared at 80°C under magnetic stirring. The dispersion was then cooled down to 40°C and, if necessary, the active ingredient was added in the specific proportion (Table 1).

The dispersion was used after at least 24 hours of rest to remove all air bubbles entrapped. The film was obtained by a laboratory-coating unit Mathis LTE-S(M) (Swissland). The aqueous dispersion was cast onto a silicone release liner with a thickness selected to obtain a placebo film with a thickness of about 120 μm. The coating rate was fixed at 1 m/min and the cast dispersion was dried in the oven at 70°C for 7 minutes with a horizontal air circulation of 1800 rpm. At the end of the preparation process, the films were cut into 3 × 2 cm strips, individually sealed in airtight packet, and stored at 25°C until use. The films were maintained over the release liner used to facilitate the packaging procedures.

Table 1. Composition (%, w/w) of the placebo and diclofenac-sodium-loaded films.

Formulation	Diclofenac sodium	MDX6	GLY	SO	Taste-masking agents: Sucralose	Mint	Licorice
Fp	—	79	18	3	—	—	—
F1	13.4	68.4	15.6	2.6	—	—	—
F2	13.4	67.4	15.6	2.6	1	—	—
F3	13.4	62.4	15.6	2.6	—	6	—
F4	13.4	61.3	15.6	2.6	1	6	—
F5	13.4	62.4	15.6	2.6	—	—	3
F6	13.4	64.3	15.6	2.6	1	—	3
F7	13.4	58.3	15.6	2.6	1	6	3

Film thickness

The film thickness was measured using a MI 1000 μm (ChemInstruments, Fairfield, OH, USA). The accuracy of the instrument was 2.5 μm ± 0.5%. A 10 × 2.5 cm sample of the film was placed between the anvil and the presser foot of the micrometer and its thickness was measured in 10 different positions. The determination process was performed in triplicate.

Tensile properties

Tensile testing was conducted using a texture analyzer AG/MC1 (Acquati, Italy), equipped with a 5 N load cell. The film was cut into 30 × 20 mm strips and equilibrated at 25°C for 1 week. Tensile tests were performed according to ASTM International Test Method for Thin Plastic Sheeting (D 882-02).

Each test strip was placed in tensile grips on the texture analyzer. Initial grip separation was 20 mm and crosshead speed was 12.5 mm/min. The test was considered concluded when the film breaks. Tensile strength, elongation at break, elastic modulus, and tensile energy to break were computed to evaluate tensile properties of the films.

Tensile strength (TS) was calculated by dividing the maximum load by the original cross-sectional area of the specimen and it was expressed in force per unit area (MPa).

Percent elongation at break ($E\%$) was calculated by dividing the extension at the moment of rupture of the specimen by the initial gage length of the specimen and multiplying by 100 according to Equation (1):

$$E\% = \frac{L - L_0}{L_0} \times 100, \quad (1)$$

where L_0 is initial gage length of the specimen and L the length at the moment of rupture.

Elastic modulus or *Young's modulus* (Y) was calculated as the slope of the linear portion of the stress–strain

curve. The result was expressed in force per unit area (MPa).

Tensile energy to break (TBE) was defined by the area under the stress–strain curve. The value is in units of energy per unit volume of the specimen's initial gage region. The result was expressed in energy per unit volume.

An average of five measurements was taken for each type of specimen.

Drug content

A 6-cm^2 sample was dissolved in an appropriate amount of the mobile phase and the solution was filtered (Durapore® membrane, pore size 0.45 μm; Millex GV, Millipore Corporation, Millipore, Vimodron, Italy) and the active ingredient assayed by high performance liquid Chromatography HPLC equipped with a diode array UV–Vis detector (HP 1100, Chemstation, Agilent Technologies, Cernusco sul Naviglio, Italy) by adapting the European Pharmacopoeia 6.4 method reported below.

A 10-μL sample was injected on a reverse-phase column (ODS Hypersil, 100 × 4.6 mm, 3 μm). The mobile phase was prepared mixing 34 volumes of 0.01M solution of sodium dihydrogen phosphate adjusted to pH 2.5 with phosphoric acid and 66 volumes of methanol. Flow rate was set at 1.5 mL/min and temperature at 45°C. DS was detected at 254 nm. The drug content was determined by a standard calibration curve represented by five known concentrations of DS ranging from 10 to 100 μg/mL (R^2 = 0.999). The results were expressed as mean of three determinations.

Disintegration test

Disintegration test was performed according to the specifications of orodispersible tablet reported in European Pharmacopoeia 6.4 edition. (2.9.1) by 6-cm^2 samples.

In vitro dissolution test

The in vitro dissolution test was carried out in a European Pharmacopoeia 6.4 edition basket dissolution apparatus. A 6-cm^2 sample of DS-loaded film was exactly weighed to assure the sink condition.

Experimental conditions. The dissolution medium was 500 mL freshly deionized water, maintained at 37 ± 1°C, and stirred at 25 rpm. DS concentrations were assayed spectrophotometrically at 275 nm (DU-640 Beckman Coulter, Cassina De' Pecchi, Italy) every 3 minutes. The dissolution profile of DS as such was also determined using the same experimental setup. The dissolution test was carried out on three samples. The dissolution results were expressed as the time required releasing 75% of loaded DS (t_{75}).

Taste evaluation

In vitro tasting system

The analyses were performed by the Taste-Sensing System SA 402B (Intelligent Sensor Technology Co. Ltd, Atsugi, Kanagawa, Japan), namely, ET. The detecting part of the system consists of sensors whose surface is attached with artificial lipid membranes having different response properties to chemical substances on the basis of their taste. In this work, three detecting sensors with positively (C00 sensor) and negatively (AC0 and AN0 sensors) charged membranes were used. All detecting sensors were specific for the evaluation of bitterness.

The measurement principle of the ET is based on the capacity of taste substances to change the potential detecting sensors through electrostatic or hydrophobic interaction with the hydrophilic and hydrophobic groups of the lipid membranes. The response of each sensor, recorded as the difference between the potential detected by the sensor electrode and the potential of the reference electrode (Ag/AgCl), is elaborated by a computer and processed through a pattern recognition system.

Figure 1 shows the measuring process applied in this work.

Detecting sensors and reference electrodes were first dipped into 60 mL of the reference solution (30 mM potassium chloride and 0.3 mM tartaric acid) and the electric potential measured for each sensor was defined

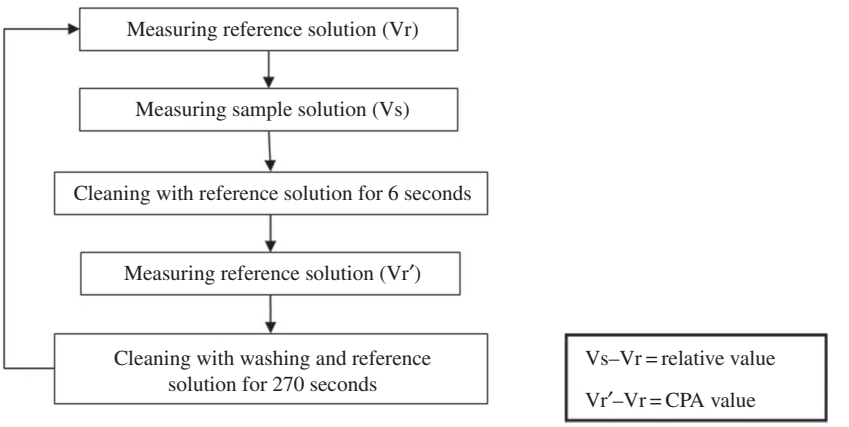

Figure 1. Measuring process by electronic tongue.

as Vr. Then, the sensors were dipped into the sample solution for 30 seconds. For each sensor the measured potential was defined as Vs and the 'relative value' was represented by the difference (Vs–Vr) between the potentials of the sample and the reference solution. Sensors were rinsed with fresh reference solution for 6 seconds and then dipped into the reference solution again. The new potential of the reference solution was defined as Vr'. For each sensor, the difference (Vr'–Vr) between the potentials of the reference solution before and after the sample measurement is the change of membrane potential caused by absorption (CPA) value and corresponds to the ET 'aftertastes'. Before a new measurement cycle started, electrodes were rinsed for 90 seconds with two washing solutions specific for positively and negatively charged membranes, and then for 180 seconds with the reference solution.

Preliminarily, the sensitivity of sensor array to DS was studied. Measurements were made on solutions at a DS concentration range (0.5–1.5%) relevant to human use and the sensor outputs (the relative value and the CPA value of each sensor) were correlated to the DS concentration by multiple regression analysis. Afterwards, solutions constituted by DS, sweeteners, and flavors were tasted by ET to select the most suitable TMAs. The tasted solutions are reported in Table 2. Finally, solutions obtained by dissolving film formulations were also analyzed. The average of two replicates was used for data analysis.

Human taste panel

The study, approved by Ethical Committee of the Università degli Studi di Milano, was conducted in accordance with the ethical principles originating from the Declaration of Helsinki and followed the ICH-GCP guidelines of the January 17, 1997 and was in compliance with local regulatory requirements. All subjects were completely informed concerning the pertinent details and the purpose of the study. A written consent form was supplied, understood, and signed by each subject prior to tasting test samples.

Aliquots of 0.50 µL solution (Table 2) were randomly tasted by 10 healthy volunteers. All samples were kept in the mouth for 15 seconds and then subjects gargled well and waited for at least 1 hour before tasting the next sample. After tasting, the volunteers were asked to value bitterness and taste sensation of solutions using a score from 0 to 4. A score of 0 corresponded to a low bitterness degree and to a palatable taste, whereas a score of 4 indicated high bitterness and worst taste sensation.

Table 2. Composition (%, w/v) of solutions tasted by volunteers and/or by electronic tongue.

		TMA					
Solution	DS	Sucralose	Xylitol	Saccharine	Mint	Licorice	Soft fruit
s1	1.34						
s2	1.34	0.1					
s3	1.34		0.1				
s4	1.34			0.1			
s5	1.34	0.1			0.6		
s6	1.34	0.1				0.6	
s7	1.34	0.1					0.6
s8	1.34				0.15		
s9	1.34				0.3		
s10	1.34				0.6		
s11	1.34					0.15	
s12	1.34					0.3	
s13	1.34					0.6	
s14	1.34	0.1			0.6	0.3	

Data processing

Principal component analysis (PCA) was applied on ET dataset. PCA is an unsupervised method used for explorative data analysis as it identifies orthogonal directions of maximum variance in the original data and projects the data into a lower-dimensionality space. The orthogonal directions are linear combinations (principal components) of the original variables and each component explains a part of total variance of the data. In particular, the first component explains the largest percentage of the total variance, the second one, the second largest percentage, and so forth[10]. PCA was performed by SCAN software (v. 1.1 Minitab Inc., State College, PA, USA). The multiple regression analysis was performed by SPSS v.11.5 for Windows®.

Results and discussion

Taste masking

Bitterness evaluation of diclofenac sodium by electronic tongue

The best correlation between the sensor data and the DS concentration was obtained considering the relative values of AN0 and C00 sensors and the CPA values of C00 sensor (CPA_{C00}). The derived multiple regression equation was: $y = 0.026AN0 - 0.030C00 + 0.055CPA_{C00} - 1696$ ($R^2 = 1.00$), where y represents the DS concentration. This result implies the usefulness of the ET to evaluate the bitterness of DS solutions at different concentrations.

Taste-masking agent evaluation by means of electronic tongue

The possibility of applying the ET to evaluate the reduction and/or masking effects of several TMAs on DS bitterness was also investigated. Measurements with the ET were carried out on DS solutions containing various sweeteners and flavors to evaluate whether the instrument was able to detect the decrease of bitterness intensity after the addition of sweeteners as well as identify their flavoring effect. The sensor outputs ('relative value' and 'CPA' value) were elaborated by PCA. To achieve a partial visualization of the dataset in a reduced dimension, PCA was performed on scaled dataset.

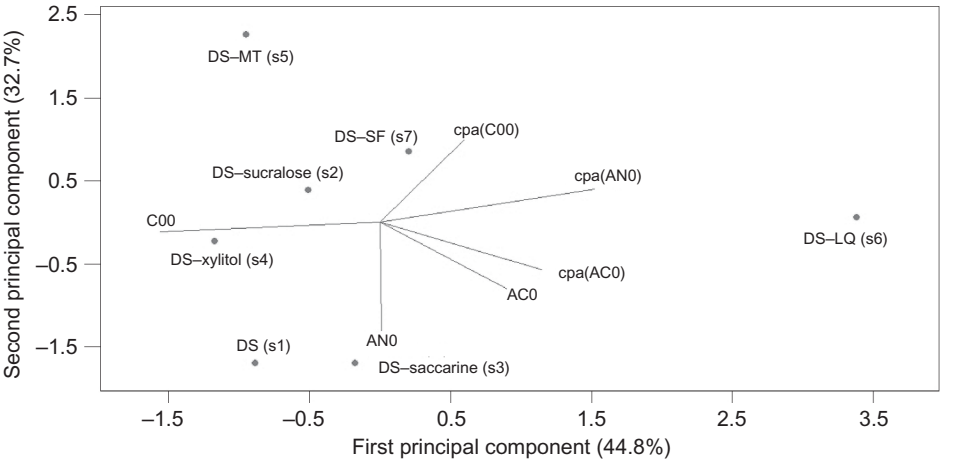

Figure 2. Bi-plot representing the electronic tongue variable (loading plot) and the samples (score plot).

Figure 2 reported the bi-plot representing both the ET variables (loading plot) and the samples (score plot) in the plane defined by the first two principal components (77.5% of total variability).

The DS solution (s1) located at left in the lower part of the plot is associated to high bitter intensity expressed by the relative value of AN0 sensor, dominant in the negative part of the second principal component, and by the relative value of C00 sensor, dominant in the negative part of the first principal component. The decrease of bitterness after the addition of sweeteners to the drug solution (s2–s4) is evident along the first and second principal component. Sucralose (s2), placed in the positive part of the second principal component masked the bitter taste of DS more effectively than saccharine (s3) and xylitol (s4) discriminated, respectively, by the AN0 sensor and by C00 sensor. Figure 2 shows also the ability of the ET to perceive the taste-masking effect of three different flavors (mint, soft fruits, and licorice) added to the DS solutions. All flavorings can be reliably discriminated by ET; moreover, PC1 and PC2 coincide with the direction in which the change of bitterness of sample occurs. In particular along PC1, licorice flavor (s6) appears on the opposite side of the plot with respect to drug solution. Discriminated by the CPA values of the sensors, it is characterized by its own bitter taste detected by the AC0 sensor. Considering the overall taste, it differs greatly by the DS solutions whereas its masking effect is explained by the lower value of C00 sensor. Along PC2, the masking effect of mint flavor (s5) is related to the lower response of AN0 sensor. The soft fruits flavor (s7) is located along PC1 between DS and licorice solutions, along PC2 between DS and mint solutions, its taste-masking effect seems to be similar to sucralose and lower than mint and licorice flavors.

The ability of the ET to evaluate the masking of bitter taste was also studied on DS solutions containing different amounts of mint flavor (0.15–0.3–0.6 g/100 mL, in s8–s10) or licorice flavor (0.15–0.3–0.6 g/100 mL, in s11–s13), compared with unflavored DS solution and DS solution added with 0.1 mg/100 mL of sucralose. The results were elaborated by PCA and Figure 3 reports the bi-plot in the plane defined by the first two principal components (84.2% of the total variance).

The unflavored DS solution is located at right in the positive part of the first and second principal component discriminated by AN0 and C00 bitterness sensors. The DS solutions added with mint flavor are located on the second principal component in a logical order reflecting the increase of mint flavor concentration and the decrease of bitter taste perceived by AN0 sensor. The DS–sucralose solution (s2) and the DS solution with 0.15 mg/100 mL of mint (s8) are located closely and are characterized by similar taste-masking effects. The DS solutions added with licorice flavor are located along the first principal component from right to left and the direction coincides with the increase of licorice flavor concentration and the decrease of bitterness as perceived by C00 sensor. The DS solution with 0.6 mg/mL of licorice (s13) appears on the opposite side of the plot and masks the drug bitter taste most effectively even if it is characterized by AC0 bitter sensor.

In a second step, the solutions prepared by dissolving the film formulations (Table 1) were analyzed. Data collected were elaborated by PCA and the bi-plot in the plane defined by the first two principal components (92.3% of total variance) is reported in Figure 4.

Moving from right to left, the first principal component coincides with the direction in which the change of bitterness of the solutions occurred. The solution composed by DS, MDX, GLY, SO (F1) is located at the right of the plot in the positive part of first principal component and it is discriminated by the relative value of AN0 and C00 bitterness sensors, the less bitter DS–sucralose film (F2) comes next. DS-loaded films flavored with mint (F3) or sucralose–mint (F4) are located further to the left and are characterized by a similar ability of masking bitter taste. Films flavored with licorice (F5) or sucralose–licorice

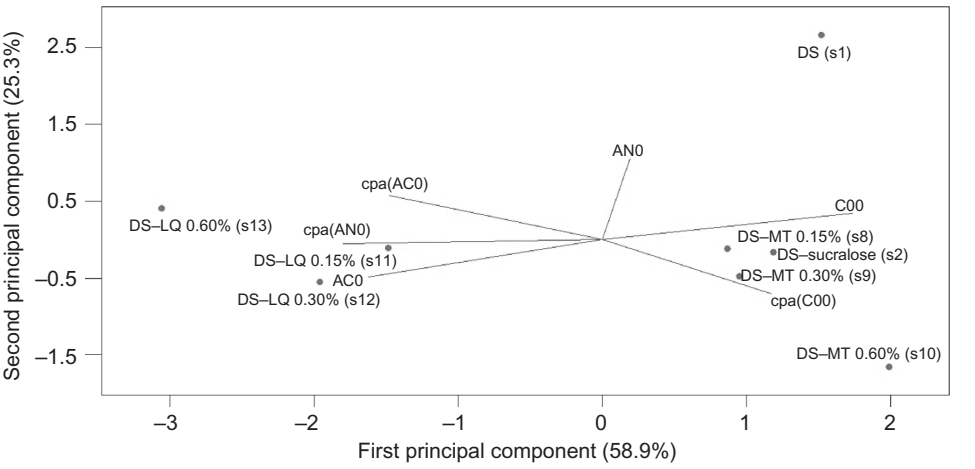

Figure 3. Bi-plot of results obtained by analyzing unflavored DS solution, DS solution added with different quantities of MT or LQ flavor and DS solution with sucralose and elaborated by PCA.

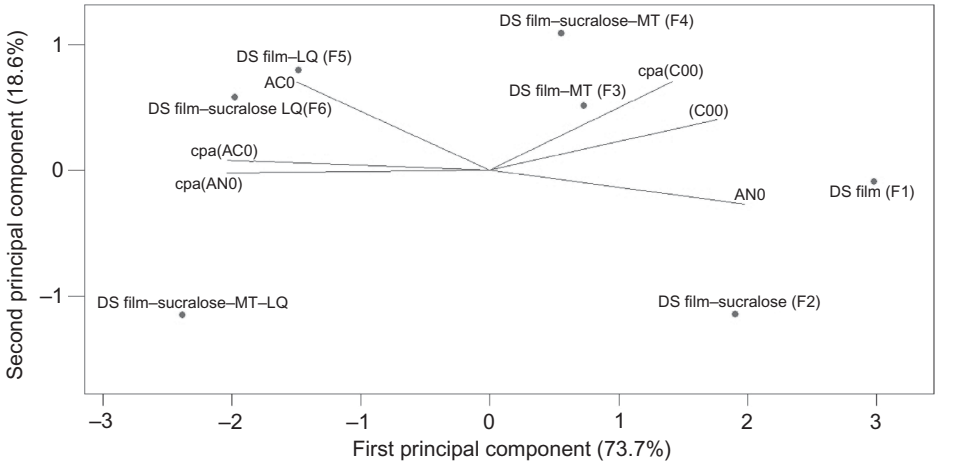

Figure 4. Bi-plot of results obtained with solutions containing all DS film components and elaborated by PCA.

(F6) located in the negative part of the first principal component, are discriminated by the relative value of AC0 sensor and the CPA values of AC0 and AN0 sensors and are characterized by a well-masked DS bitter taste. On the opposite side of the plot, the DS film including sucralose–licorice–mint (F7) is less discriminated by both AN0 and C00 bitterness sensors and masks the drug bitter taste most effectively.

Human taste panel

The in vitro results obtained by ET and the sensory properties of the DS-sweetener solutions evaluated by the sensory panel were compared (Table 3). The ET scores are represented by the Euclidean distances between the DS solution (s1) and the formulations added with sweeteners (s2–s4) and/or flavors (s5–s13) measured on the PCA score plots reported in Figures 2 and 3. Each contribution, weighed by considering the explained variance on the first two principal components, represents an index of dissimilarity between DS solution and the formulations added with TMAs. The data were interpreted by assuming that a formulation is well taste

Table 3. Evaluation of bitterness and taste sensation by volunteers and electronic tongue.

	Human taste panel (scores)		Electronic tongue (scores)
Tasted solutions	Bitterness	Taste sensation	Dissimilarity index
s1	3.6	3.3	0
s2	2.3	2.9	0.69
s3	3.5	3.4	0.52
s4	3.0	3.2	0.32
s5	2.3	1.5	1.30
s6	1.6	1	2.17
s7	2.3	3.1	0.97
s10	2.6	2.6	1.12
s13	2.0	2.7	2.06
s14	1.7	0.5	—

masked if it is recognized by the ET dissimilar from the DS solution. In particular, the larger is the Euclidean distance, the higher is the dissimilarity index between DS solution and TMA formulation and consequently the greater is the masking effect of sweetener or flavor.

As it can be seen in Table 3, the human and the ET scores are in agreement. Among the selected sweeteners at the fixed percentage, the DS–sucralose solution (s2), perceived as the least bitter and with the most acceptable taste by the sensory panel, is characterized by the highest dissimilarity index. The addition of mint flavor (s5) or licorice flavor (s6) improved the taste of the DS–sucralose solutions. The comparison of s5 to s10 and s6 to s13 evidenced that sucralose was required to improve taste for volunteers, in agreement with the ET scores. By considering the sensory panel, sucralose–mint–licorice solution (s14) appeared the most suitable combination to mask the DS taste.

Fast-dissolving film technological characterization

All films appeared homogeneous upon a visual inspection, flexible, and not brittle. They were handled, cut, and packed without any failure. The films weighted in the 95–110 mg range and the DS content in each formulation (Table 4) ranging 85–115% of the mean value complied the drug content assay according to the Ph. Eur. and consistent with the theoretic drug loading, namely 13.4 mg.

The comparison of Fp and F1 in terms of tensile properties showed that the presence of DS modified the mechanical properties of films, determining a decrease of plasticity (Table 4). Figure 5 shows force-deformation curves for the placebo films (Fp) and the DS-loaded film (F1). The portion of the curves at lowest stress appeared linear and the deformation of the samples was elastic. The Young's modulus, that is an index of stiffness, was higher for the formulation F1, because of the presence of insoluble drug substance. Increasing the strain, the deformation became plastic and values of maximum load reached by the samples were not significantly different. This feature implies that the films had a comparable strength at deformation stress. After tensile strength points, the curves became significantly different. F1 was characterized by lower value of elongation at break that expressed the ductility of the film. For both formulations with increasing strain the stress decreases; neck formation and neck growth were observed, but this behavior was more evident for Fp. Finally also the toughness, expressed as the tensile energy to break, resulted reduced by drug substance addition. Placebo formulation,

Table 4. Drug content (%, w/w), disintegration time (Tdis), thickness, and mechanical properties of placebo and diclofenac–sodium-loaded films.

				Mechanical properties			
Formulation	Drug content (%, w/w)	Tdis (seconds)	Thickness (μm)	Y (MPa)	TS (MPa)	E (%)	TBE (kJ)
Fp	—	14 ± 2	128 ± 6	0.212 ± 0.087	1.580 ± 0.409	75.37 ± 8.58	40.0 ± 15.6
F1	13.1 ± 0.1	13 ± 1	119 ± 6	0.839 ± 0.118	1.805 ± 0.060	30.57 ± 3.04	17.7 ± 1.3
F2	13.4 ± 0.1	12 ± 2	120 ± 3	0.261 ± 0.080	0.528 ± 0.116	56.96 ± 6.60	11.0 ± 0.3
F3	13.0 ± 0.2	11 ± 2	125 ± 4	0.380 ± 0.100	0.876 ± 0.114	57.80 ± 9.80	15.4 ± 4.1
F4	13.8 ± 0.4	12 ± 1	113 ± 8	0.130 ± 0.020	0.460 ± 0.040	157.10 ± 17.20	14.3 ± 1.7
F5	14.1 ± 0.2	12 ± 1	117 ± 1	0.118 ± 0.095	1.297 ± 0.118	54.04 ± 11.31	18.4 ± 2.1
F6	13.3 ± 0.3	10 ± 1	123 ± 5	0.043 ± 0.010	0.733 ± 0.070	86.44 ± 13.56	25.7 ± 2.1
F7	14.3 ± 0.3	16 ± 1	124 ± 6	0.234 ± 0.084	0.957 ± 0.186	30.77 ± 2.57	9.4 ± 0.5

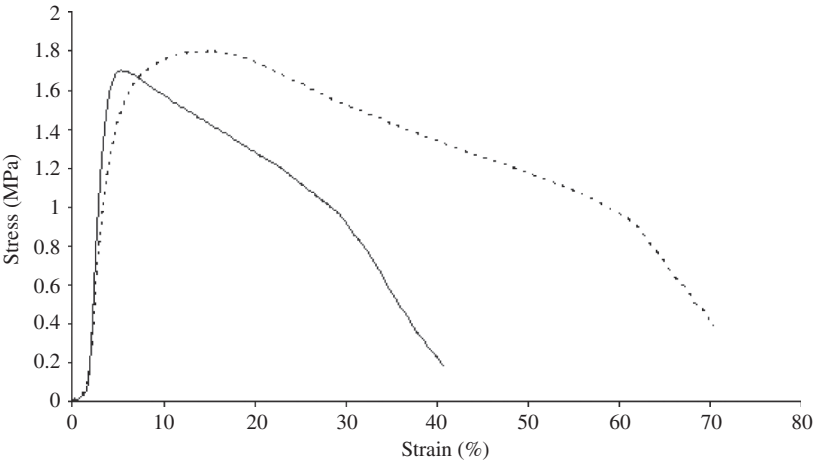

Figure 5. Strain–stress curves of the placebo formulation, Fp (dotted line) and DS-loaded film, F1 (solid line).

therefore, resulted more ductile and the addition of the drug substance led a decrease of deformation of film when subjected to a stress. These data resulted consistent with those previously described for piroxicam[2] suggesting that the addition of large amount of drug determines an increase of the stiffening of the MDX film, independently of the DE value of the used MDX.

Drug-loaded films containing TMAs exhibited substantially a higher plasticity compared to F1. The increase of ductility and the decrease of tensile strength complemented each other, so the values of toughness did not significantly change. The addition of the selected TMAs compensated for the anti-plasticizing effect of the drug substance.

Drug-loaded as well as placebo films disintegrated in few seconds. The in vitro dissolution test revealed that the loading of the DS within the film minimally affected the drug dissolution rate. Indeed, the t_{75} of DS raw material resulted 3 minutes, whereas the t_{75} of F7, comprising all the selected TMAs, was in the 4–6 minutes range.

Conclusions

The taste sensor system, that is, ET, represents a useful tool to evaluate the feasibility to suppress the drug bitterness by TMAs during the development of fast-dissolving films. This system can allow discriminating the effect of the TMA also in presence of the other hydrosoluble constituents of the film, namely polymers and surfactants. As the ET presents the advantages of simplicity and rapidity, this technique could assist or even replace the sensory evaluation in the development of new pharmaceutical formulations providing information about the taste without the need of humans to taste active compounds.

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Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of this paper.

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