

Formulating better tasting pediatric drug is just as important as better adherence. The development of drug that are easily taken orally is very important especially for pediatric or geriatric patients, as is the efficiency of drug. We would like to introduce 3 cases of drug formulation development work by Japanese pharmaceutical company(originator) for which our taste sensing system played an active role in taste adjustment between placebo and active drug or finding appropriate bitterness masking agent for the API.

Case 1:

Taste tuning of Placebo and Active drug for clinical trial at an early phase of development.

Background :

Simplified Formulation like solution or suspension is commonly applied for Clinical trial rather than producing complex solid dosage form at early phase of development stage. API's taste in simplified formulation is directly exposed, so it is required to formulate the taste of placebo and active drug as similar taste as possible for a more reliable clinical trial. It is difficult to know the taste of API at early phase of development due to its safety aspect. This is an example of how our customer use the system for this kind of work.



Taste sensing system TS-5000Z

Application :

The company developed new API which has Free form and Phosphate form. The taste of Free form is stable at any concentration although they observe Phosphate form has bitterness and sourness(Fig.1).

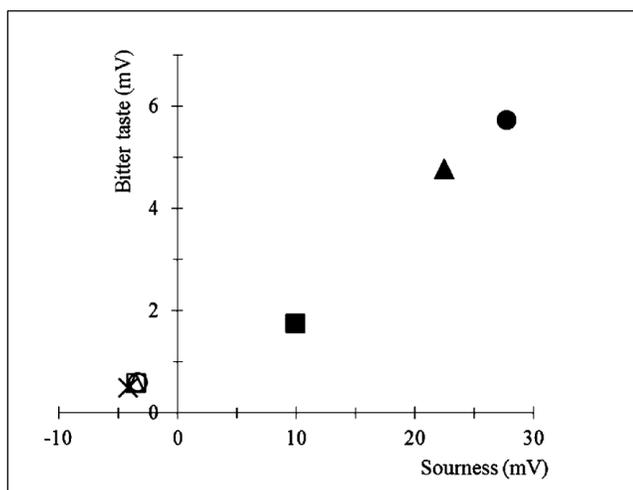


Fig.1 Sourness and Bitterness sensor outputs of suspension of New drugs under Early Phase of Development.

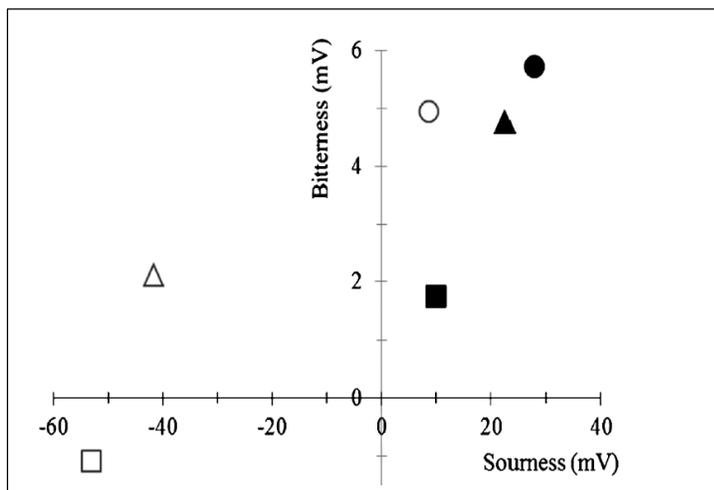


Fig.2 Sourness and Bitterness sensor outputs of Suspensions of New drugs and Placebo solution

Suspension base(x), Free form drug in low conc(□),
 in moderate conc(Δ), in high conc(o)
 Phosphate drug in low concentration(■),
 in moderate conc(▲), in high conc(●)

Citric acid solution in low concentration(□),
 in moderate conc(Δ), in high conc(o)
 Phosphoric drug in low concentration(■),
 in moderate conc(▲), in high conc(●)

From the result of (Fig.1), it is suggested that salt form affects to taste of suspension rather than API's own taste. (Fig.2) is showing the bitterness and sourness intensity of various concentrations of citric acid solution and Phosphoric drug solution. They show similar taste tendency that assures the similar taste profile of placebo and active drug.

Case 2 :

Taste masking of API in jelly dosage drug

Background :

Jelly dosage is sometimes chosen as an effective dosage form for geriatric or people who has difficulty in swallowing. In general, taste masking of jelly form is more difficult than solid dosage form as masking method is limited. They tried to apply a polysaccharide to reduce bitterness of API.

Application :

(Fig.3) is showing bitterness sensor response to 0.2% of different polysaccharide added with 0.04% API. It is suggested that Carrageenan can reduce bitterness of API effectively in order ι , λ and κ type.

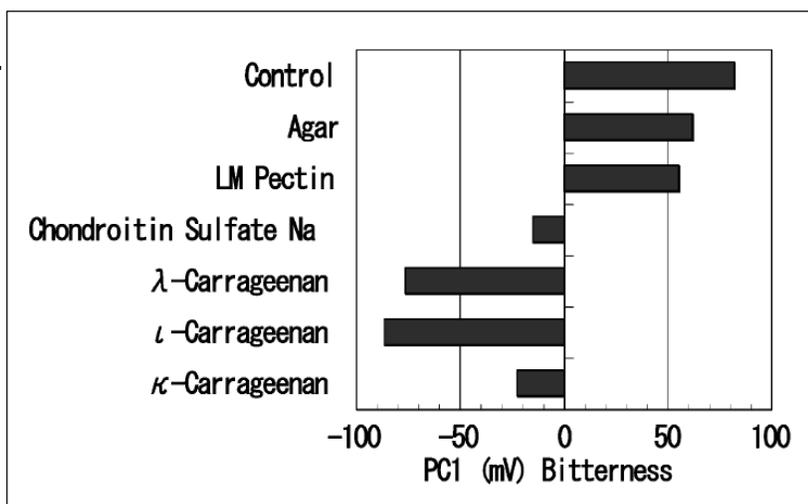


Fig.3 Effect of Masking Agents on Donepezil Hydrochloride solution

They consider interaction between cationic API and anionic polymers leads API's molecular weight growth, then it reduces chance in bonding to taste bad on human tongue (lipid membrane in sensor).

(Fig.4) is showing taste stability test of 3, 5 and 10mg API contained jelly dosage drug. The control and 36months stored at 5 degree C are tested. In addition, 0.01, 0.1 and 1mM API solution are measured to compare.

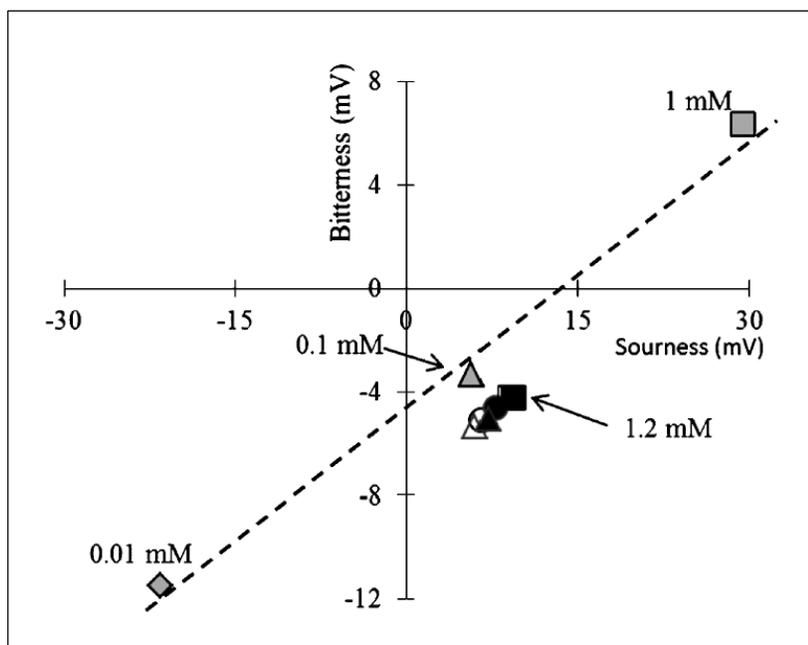


Fig.4 Sourness and Bitterness Sensor Outputs of Stability Sample for 36months of ARICEPT Oral Jelly Formulation and Donepezil Hydrochloride solution
 3mg/5°C(o), 3mg/25°C(●), 5mg/5°C(Δ),
 5mg/25°C(▲), 10mg/5°C(□), 10mg/25°C(■)

What is Taste sensing system?

Employs the same mechanism as the human tongue to measure initial & aftertaste through artificial lipid membrane sensors that interpret taste reception of drugs, beverages or foods as numerical data.

What is different between chemical analysis and taste sensing system?

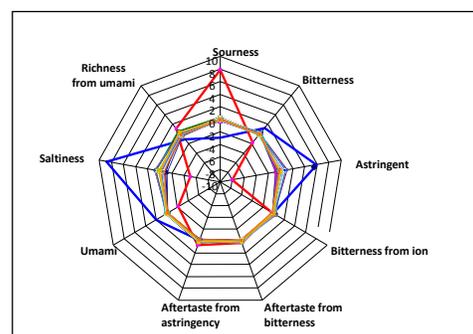
It is not realistic to express taste by chemical analysis. For example, it is said that hundreds of substances are contained in coffee that contribute to its taste. HPLC can give us precise answer in quantitative and qualitative number of them but it is difficult to convert those data into numerical taste information. For example, even though the amount of caffeine(bitterness level) is the unchanged, the bitterness level seems to change after adding in the sugar. The amount of bitterness has not changed, but the taste can change depending on what is in the mix. This is called taste interaction. Taste sensing system can measure taste interaction. That is the reason it is widely applied in pharmaceutical company who requires measurement of taste suppression or enhancement.

How many sensors are used?

We can measure 5 basic tastes and Astringency. Umami(Savoriness), Bitterness and Astringency can be measured for initial and aftertaste separately. The sensor is the most unique feature in this system. There are 8 sensors available corresponding to each taste. Each sensor selectively responds to each taste and sensor output is adjusted with human threshold and intensity. There are 3 different bitterness sensors, one is mainly used for food or drug and two are used for mainly drug.

What kind of drug or food can the system measure?

Any sample can be measured, as long as it is in liquid form. When testing drugs, we usually dissolve API or drug in 10mMKCl solvent to give it some conductivity. When testing foods, we usually use purified water to dissolve or mix with samples to extract the taste. Removal of oil to less than 2% is recommended for optimum sensor conditions.



How long does it take for measurement?

40 minutes per one sample. 90% of the total time is consumed for sensor washing and sensor stabilization.

Is there any sample which the system cannot measure?

Neutral substances. The sensor reads electric potential difference sensor and Reference electrode. The principal is similar to mechanism of human taste sensory.



References: YAKUGAKU ZASSHI 134(3)325-331(2014)

Disclaimer: This information is for reference only, and is not proof of absolute taste quality of samples, nor guarantee data repeat-ability.

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