The human descriptive sensory panel - a tool for understanding how bitter taste is impacted during formulation

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1 INTRODUCTION & AIM

Methodologies that assess the contribution of formulation components to a medicine's overall sensory profile are valuable when optimising the design of patient-acceptable drug products. Assessing a medicine's sensory profile is of particular importance for oral formulations containing bitter-tasting drugs which can undermine patient adherence. This study aims to illustrate how a human descriptive sensory panel can be used to assess the sensory characteristics of oral formulation components and products. The data presented is historical trial data.

2a METHODS - Establishment of a Human Descriptive Panel

Phase 1

.: selection of panellists :.

Initial screening of potential panellists via phone interview & requirement to pass inclusion/exclusion criteria to progress

Acuity screening of potential panellists using ISO8586-1: 1993-03-15

- Basic taste detection, ID & intensity
- Odour detection and ID
- Discrimination testing
- Ranking
- Scaling
- Descriptive & communication ability

Medical assessment & clearance

Phase 2

.: Sensory training

Particular emphasis on bitter taste - performance assessed throughout training

- Individual performance indicators measured - reproducibility, discrimination & agreement with the panel average
- Group performance measured - reproducibility & discrimination

2b METHODS – Formulations

Model bitter compounds caffeine, quinine (base (QB) and HCl salt (QHCl)) & sucrose octaacetate (SOA).

Formulation approaches.

1. QHCL and Caffeine: Suspensions of spray-dried particles containing Eudragit E PO™ and sodium casein.
   Ratio Caffeine:E PO™:Casein *1:4.5:0.45*
   Ratio QHCl:E PO™:Casein *1:185:18.5*

2. QB and SOA: Microemulsions formed self-micro-emulsifying drug delivery systems (SMEDDS)

SMEDDS	Surfactant 1 (%)	Surfactant 2 (%)	Surfactant 3 (%)
#1	Labrafil (40)	Tween 80 (20)	Cremophor RH40 (40)
#2	Miglyol (21)	Tween 85 (49)	Cremophor RH40 (30)
#3	Labrafil (56)	Tween 85 (14)	Cremophor RH40 (30)
#4	Miglyol 812 (42)	Crill 1 (28)	Cremophor RH40 (30)
#5	Miglyol 812 (42)	Caprol PGE 860 (28)	Cremophor RH40 (30)
#6	Miglyol 812 (39)	Tween 85 (26)	Cremophor RH40 (35)

2c METHODS – Panel Formulation Assessment

Absolute threshold concentration of the trained human taste panel for QHCL, SOA and caffeine determined

Particle dose (equivalent to a multiple of the compound's threshold bitter concentration), SMEDDS and surfactants administered dispersed in 30mls of water

Attributes of the samples were identified, and the intensities quantified using a 10 cm scale. Samples were evaluated in triplicate by a minimum of 8 panelists.

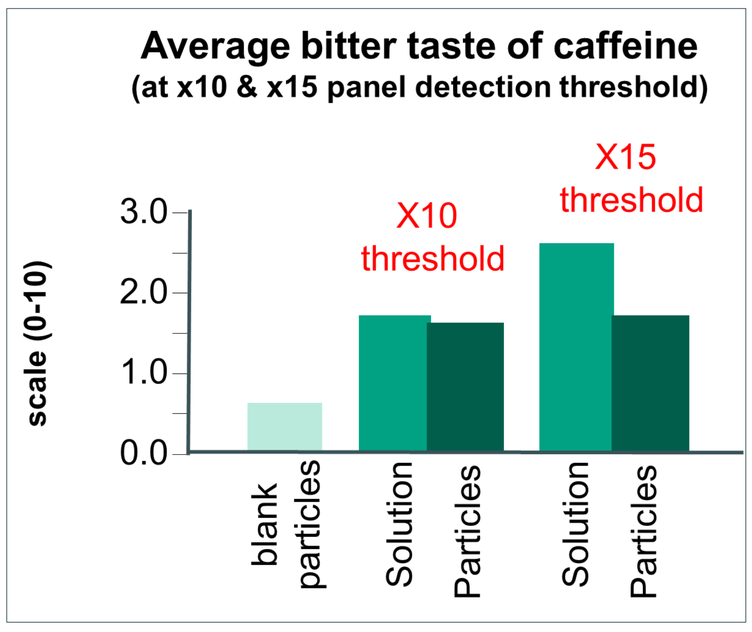
3 RESULTS

Panel average bitter threshold concentrations for model compounds

Compound*	Threshold
Caffeine	54.4 µg/ml
QHCL	1.4 µg/ml
SOA	0.7 µg/ml

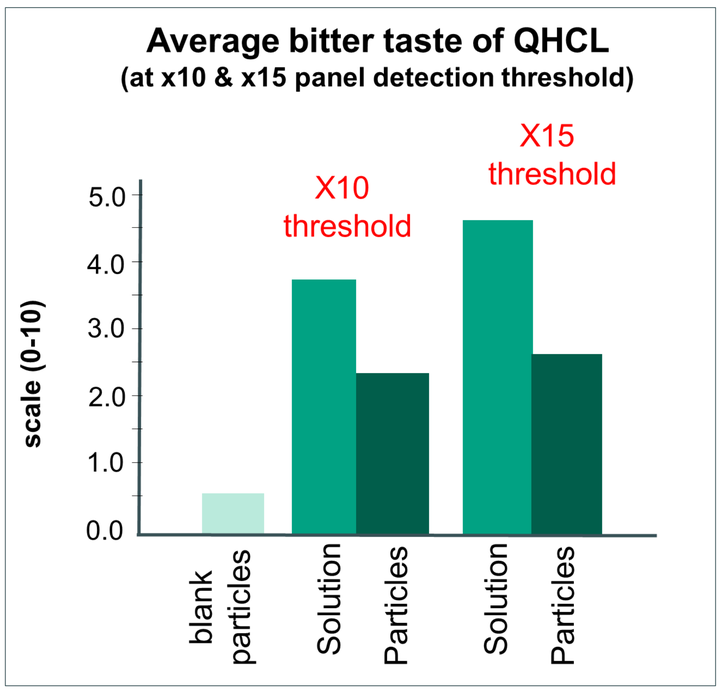
*The threshold concentration of quinine base in solution was not measured as it was considered to be equivalent to that of quinine HCl. This assumption was made as it is the quinine molecule in solution that causes the bitter taste sensation.

Suspensions of spray-dried particles



Novel solid dispersion microparticles containing model bitter compounds, had a reduced bitter taste, compared to the same dose of bitter compound given as an oral solution and tasted by a trained sensory panel.

The bitter taste reduction was more evident for the quinine HCl/Eudragit EPO™ microparticles compared to caffeine/Eudragit EPO™ .

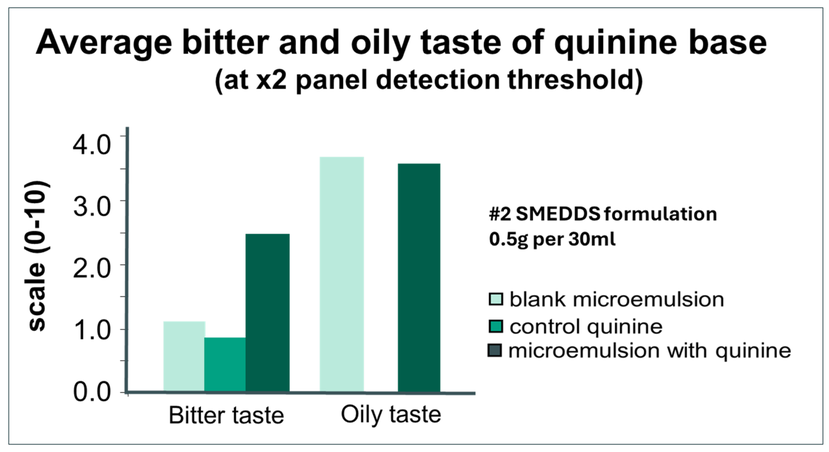


Microemulsions formed from SMEDDS

Formulation Microemulsion #	Panel Assessment *sensory attribute measured* Overall taste	Oily taste	Bitter taste
#1 blank (1g in 30ml)	Very strong chemical taste (dried blood, iron)		4.0
#2 blank (0.1g in 30ml)	2.5	2.8	0.6
#2 blank (0.5g in 30ml)	3.3	3.9	1.2
#3 blank (0.5g in 30ml)	4.2	3.4	1.3
#4 blank (0.5g in 30ml)	5.8	3.5	2.4
#5 blank (0.5g in 30ml)	5.8	4.7	2.5
#6 blank (0.5g in 30ml)	4.5	3.2	1.5

- All microemulsions investigated had a strong overall, oily and bitter taste (scale 0-10).
- The taste of individual surfactants included in the formulations was assessed. The panels' overall taste response was similar, but the descriptors differed.
- The overall taste of all surfactants ↑ as the concentration of the surfactant in solution ↑.
- The microemulsion using SMEDDS #2 was selected and its ability to mask the bitter taste quinine base (using twice the bitter threshold concentration (2.8 µg/ml) was investigated.

Surfactant (0.5% w/v)	Panel Assessment *sensory attribute measured* Overall taste	Description
Cremophor RH40	3.1	Slight oily, dry, salty
Tween 80	3.6	Dry, oily, reminiscent of liquid paraffin
Tween 85	3.7	Oily, reminiscent of liquid paraffin
Crill 1	3.8	Soapy and slightly oily and bitter, strong after taste
Caprol PGE 860	3.6	Slightly oily, soapy and bitter, strong after taste



Microemulsions prepared from SMEDDS systems did not reduce the bitter taste of quinine base or sucrose octaacetate (results not shown) and therefore are unlikely to be suitable as oral liquid dosage forms to mask the bitter taste of poorly water-soluble drugs.

4 DISCUSSION/CONCLUSION

The use of a human sensory panel to understand the sensory impact during formulation and its components provides meaningful direction throughout the formulation development process.

Further work using model compounds and taking a hybrid human panel approach (i.e., combining both analytical measurements of key sensory attributes & palatability measurements) may further help to formulate palatable medicine.

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