Veterinary soft chews using Gelucire® 50/13 and Precirol® ATO 5. A proof of concept with wet extrusion

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INTRODUCTION

Veterinary soft chews are gaining interest among oral dosage forms for companion animals as they provide good acceptance for the pet and are easy to administrate by the pet owner, ensuring better compliance to the treatment. For the veterinary laboratory, it offers many advantages such as a simple process and an easy dosage scale-up. Soft chews are also suitable for many APIs: liquid or powder, hydrophilic or lipophilic, heat and water sensitive.

This dosage form also enables to achieve high drug load, taste masking ability, sustained or immediate drug release. This new dosage form also contributes to product life cycle management.
The aim of our study was to demonstrate how our Gelucire® 50/13 surfactant, and Precirol® ATO 5, taste-masking agent, can be used in soft chews prepared by wet extrusion process.

MATERIALS AND METHODS

The flavor used was the Artificial Powdered Meat Flavor PC-0170 from Pet Flavors. The filler was Maize Starch B from Roquette and lactose Pharmatose® 200M from DFE Pharma was used as a diluent. Gelucire® 50/13, stearoyl macrogol-32 glycerides EP from Gattefossé was used as a surfactant. Precirol® ATO 5, glycerol distearate (type I) EP from Gattefossé was used as a thickener and taste-masking agent. Glycerol and oil (Maisine® CC, glycerol monolinoleate EP from Gattefossé) were used as liquid components of the formulation.
The trials were performed on a Pharma 16 twin-screw extruder from Thermo Scientific (Karlsruhe, Germany), equipped with 4 different feeders: two gravimetric feeders for feeding pellets and powder, and two volumetric liquid pumps for feeding oil and glycerol. The screw configuration was adjusted for the soft chews with 3 short kneading blocks, a reverse element, and short helix feed screws to ensure good mixing of all components and compounding. The screw speed was 300 rpm, and extrusion was performed at 25°C. The die was an 11*6 mm ellipse. A pneumatic cutter was set at the die exit.
The composition of the formulations was adjusted according to the actual throughputs of the different feeders and varied to investigate the impact on the soft chew texture. Figure 1 shows the global median composition of the soft chews and Figure 2 the extent of variations in composition of the experimental formulations, in agreement with the soft chew composition available in literature[1].
The soft chews were evaluated for appearance and hardness, after a stabilization period of 7 days after manufacture, using a texture analyzer Chatillon TCM 100 (n=10).

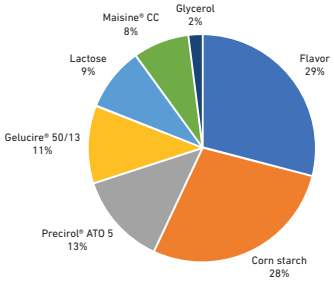

Figure 1. Global median composition of experimental soft chews.

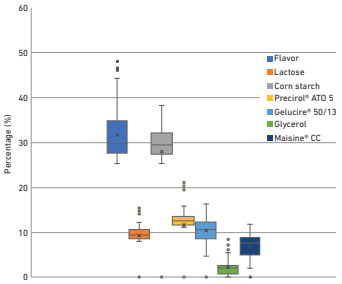

Figure 2. Extent of variations in experimental soft chews composition.

RESULTS AND DISCUSSION

Setting extrusion parameters for optimal soft chew appearance
With independent adjustment of the throughputs of each feeder, it was very convenient to adapt the composition depending on the appearance of the soft chews at the die exit. For instance, when the soft chews were too sticky, a slight reduction of the glycerol content enabled to solve the issue. On the other hand, when the surface of the soft chew was oily, a reduction in the oil throughput was necessary.
The extrusions were consistently performed at 25°C, and only the mechanical energy in the kneading zones generated some limited heat, which was detected at the end of the barrel right before the die, using a pressure probe.
A link was observed between material temperature and hardness of the soft chews (Figure 3). Hardness reached 40 to 80 N, equivalent to the market references, when the material temperature at the die was between 36 and 42°C.

Effect of excipients and their concentration on the texture of soft chews
With the market references' hardness being between 40 and 80 N, we focused on the experimental formulations able to reach equivalent hardness (Table 1). The surfactant Gelucire® 50/13 could be used at 9 to 15% in these formulations. When used at about 13-15%, Precirol® ATO 5 provided nice texture and appearance to the soft chews. Especially, a nice and glossy appearance was obtained. Without Precirol® ATO 5, soft chews of appropriate hardness and appearance were also obtained.
If soft chews could successfully be produced without lactose or without starch in the formulation, the hardness was in the lower range of about 45 N. Without corn starch, the surface of the soft chews was very grainy.
We noticed that only a very small quantity of liquid (1-3%) was necessary to form the soft chews. When the quantity of liquid was higher, sticky or oily soft chews were obtained. On the other hand, with a limited amount of liquid, the pressure in the extruder and hence the material temperature at the die was slightly higher, which enabled the production of harder soft chews.

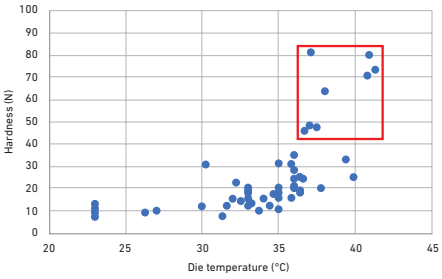

Figure 3. Effect of material temperature detected at the die on soft chew hardness.

Table 1: Composition and process parameters of soft chews with acceptable hardness.

Composition (%)	Flavor	32	31	36	35	46	38	36
	Lactose	10	10	0	0	15	12	12
	Corn starch	32	30	36	34	0	38	36
	Precirol® ATO 5	14	13	16	15	20	0	0
	Gelucire® 50/13	11	15	9	13	16	11	15
	Glycerol	1	1	1	1	1	1	1
	Maisine® CC	0	0	2	2	2	0	0
Flow (g/h)	Powder	1000	1000	1200	1200	1200	1000	1000
	Pellets	120	180	120	180	240	120	180
	Glycerol	7	7	8	8	8	8	8
	Oil	0	0	30	30	30	0	0
Extrusion parameters	Screw speed (rpm)	300	300	300	300	300	300	300
	Die temperature (°C)	37.1	38	36.7	37.5	37	41.3	40.9
	Pressure (bar)	6.3	6	8	6.3	11	6.6	6
Soft chews	Hardness (N)	79	65	46	47	44	77	77
	Appearance							

CONCLUSION

This experimental study is a proof of concept highlighting the possibility to prepare veterinary soft chews by wet extrusion, using Gelucire® 50/13 as surfactant at about 10-15%. This excipient has precedence of use in human and veterinary medicines and is an acknowledged bioavailability enhancer. Precirol® ATO 5 is a GRAS excipient, and a reputed taste-masking agent with precedence of use in human and veterinary medicines. It can be added in soft chews at high level, contributing to API taste masking and to the overall acceptance of the dosage form by the pet.
To our knowledge this study is the first to demonstrate the potential of lipid excipients in veterinary soft chews. Further work is necessary to evaluate the stability of the products and tests with a model drug should be carried out to evaluate the release from this dosage form.

REFERENCE

[1] Susi Alteheld, Stefan Fuchs, Carina Hang, Jürgen Lutz. Soft chewable pharmaceutical products. Patent US 2019/0201332, 2019.