Protection and Processing of a Highly Hygroscopic Herbal Extract by Drug Layering and Film Coating

OBJECTIVE

To stabilize a highly hygroscopic herbal extract in a solid dosage form using a drug layering process followed by a moisture barrier film coating.

INTRODUCTION

The majority of modern herbal extracts are prepared by an alcohol/water extraction method which tends to give them a hygroscopic nature. This can make it difficult for the extract to be processed into a solid dosage form and stabilized under normal storage conditions. This project evaluated the use of a drug layering process and moisture barrier film coating to produce stable active beads for filling into hard gelatin capsules.

Echinacea purpurea (Purple Coneflower) is used widely in the US and Europe as an herbal medicine for its immunostimulant activity. As a result of the European Traditional Herbal Medicines Directive from 2011, all herbs on the European Market must be licensed and meet strict pharmaceutical standards. The use of this technique may make it easier to meet the new stability requirements.

METHODOLOGY

Materials

Echinacea dry pressed juice EFLA® 894 (Flachsmann)

Marker compound b-1,2-D-fructofuranosides > 2.4%(m/m)

Fumed silica (Aerosil® 200, Degussa)

MCC beads (Ethispheres® 600 (600 mm, NP Pharm)

Opadry®, complete film coating system (20A29073 Clear) and Opadry II, high performance film coating system, (85G66695 Brown)

Equipment:

Niro Aeromatic Strea 1 using the bottom spray set up with a 1mm nozzle

Watson Marlow peristaltic pump.

Ika RW20.n stirrer. Sartorius 4 digit balance.

Orion Research Inc. AF8 Titrator. Olympus SZ Microscope.

Olympus C3030 zoom digital camera.

Process

An aqueous suspension of powdered echinacea purpurea extract and silicon dioxide was sprayed onto non-pareil MCC beads to 67% weight gain in a fluid bed processor using a bottom spray module. Silicon dioxide was added to the formulation to reduce the stickiness of the beads during the layering process. Moisture barrier film coatings (Opadry 20A29073 or Opadry II 85G66695) were then applied to a 5% weight gain in the same manner.

Formulation

The German Commission E Monograph[1] recommends a dose of 6-9 ml of pressed juice, taken from the aerial parts of the plant. This is equivalent to 320 mg of Echinacea purpurea Pressed Juice Extract (EFLA®894), the formulations used deliver a dose of 6 ml of pressed juice per daily dose.

Table 1. Echinacea purpurea bead formulation

	1Kg Batch	Per 500 mg Capsule*	640.5 g Batch	Per 320 mg Capsule**
Echnacea purpurea	640 g	320 mg	320 g	160 mg
Pellet Cores (600 µ m)	270 g	135 mg	270g	134.752 mg
Silicon Dioxide	40 g	20 mg	20 g	10.016 mg
Opadry	50 g	5 mg	30.5 g	15.232 mg

*One capsule per day formulation.
** Two capsules per day formulation.

Table 2.

	20A29073	85G66695
Drug Layering		
Atomizing Air Pressure (bar)	2.5	2.5
Inlet Air Temperature (ºC)	60-67	60-67
Fluid Delivery (g/min)	2.5	2.5
Solids Content (%)	58	58
Film Coating		
Atomizing Air Pressure (bar)	2.0	2.0
Inlet Air Temperature (ºC)	50	50
Fluid Delivery (g/min)	3-4	3-4
Solids Content (%)	15	20

Extract Characterization

Samples of the extract were placed on a glass petri dish and left at room temperature and humidity. Visual observations were made at time 0, 3 and 6 hours. Water absorption by dried extract samples was also evaluated. Samples of high drug loaded beads were placed in clear PVC containers with plastic cap for visual observations after 18 months of storage at room temperature and humidity.

Stability Study

Samples (3 g) of extract powder and the high and low dose beads were dried in an oven for 2 hours at 105°C. Smaller samples (0.1g) of each material were then transferred into a clear glass vial (28 mL) and placed on stability for 7 days at 25ºC and 60%RH for a moisture absorption test.

The high drug loaded beads were also filled into hard gelatin capsules with a 500 mg capsule fill weight and packed in heat induction sealed HDPE bottles for stability storage. The weight of filled capsules, moisture content of beads by Karl Fischer, and appearance of capsules/beads were determined through the 18 month time point under ICH storage conditions.

RESULTS

Extract Characterization

Figure 1. Visual Observation of Extract Powder at Room Temperature and Humidity, Approximately 20°C and 40-50%RH.

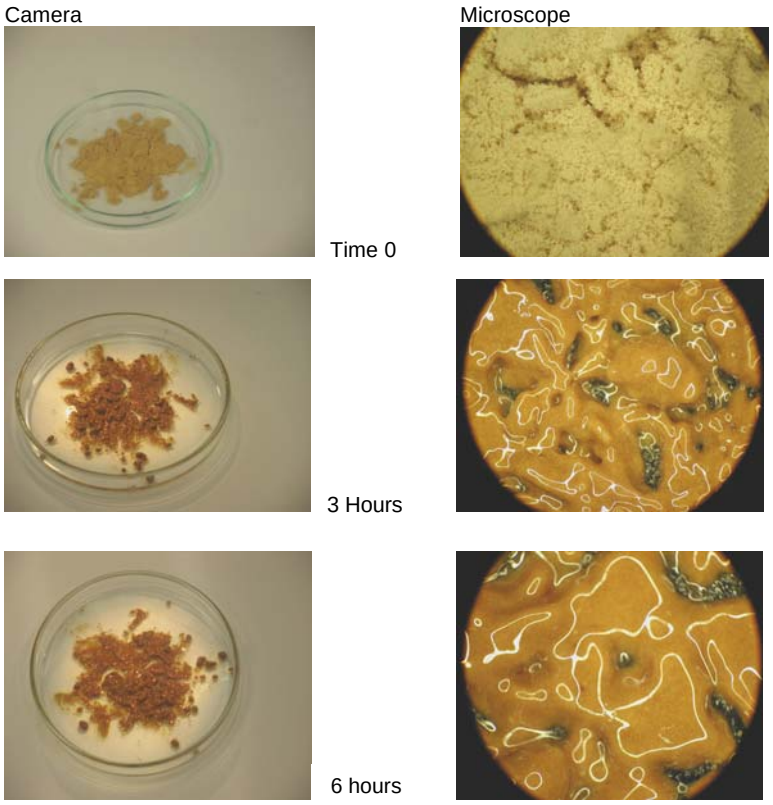


Figure 2. Weight Gain of 5g Extract Sample Dried at 90C for 18 hours and then Stored at 40ºC 75%RH for 2 days

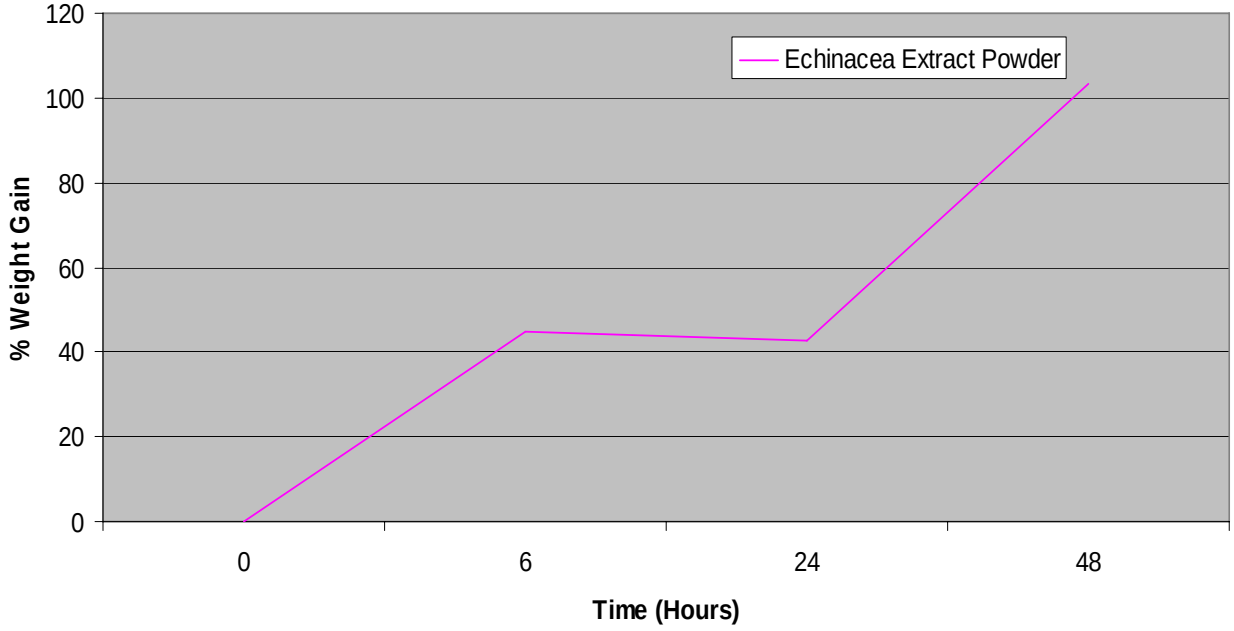
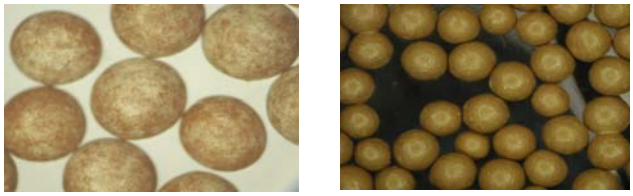
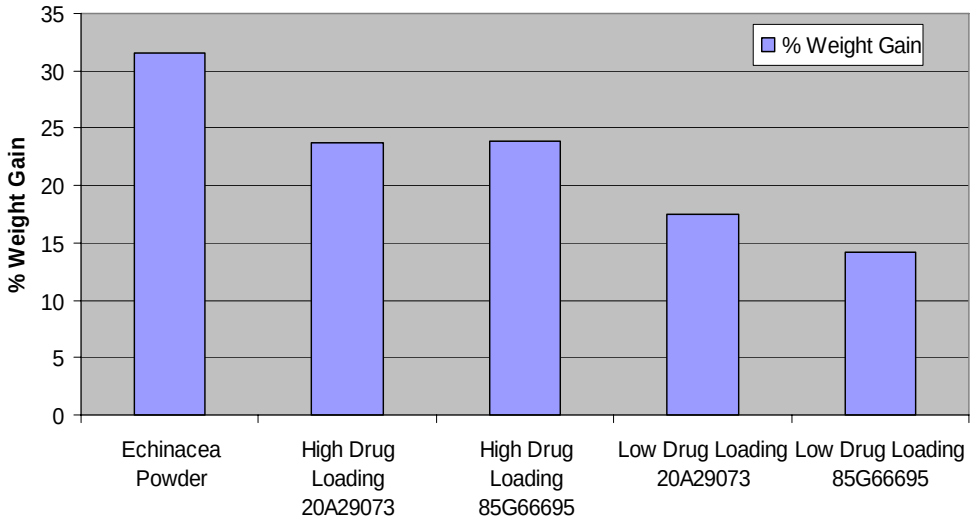


Figure 3. High Drug Load Formulations: Free Flowing Beads after 18 Months in PVC Container at Room Temperature & Humidity



Opadry 20A29073 Clear Opadry II 85G66695 Brown
Both coatings applied to 5% weight gain.

Figure 4. Percentage Weight Gain (Equilibrium Moisture Content)[2] after Dried Samples Stored at 25°C and 60%RH for 7 days



The equilibrium moisture content (EMC) was highest for the echinacea powder. EMC increased with increasing loading of echinacea onto the beads.

Table 3. Karl Fischer Results for Echinacea Bead Capsules Packed in HDPE Bottles.

	20A29073 Initial	85G66695 Initial	20A29073 3M	85G66695 3M
25ºC/60%RH	4.89 +/- 0.12	5.83 +/- 0.49	5.10 +/- 0.99	6.06 +/- 0.82
30ºC/65%RH			6.64 +/- 0.58	6.15 +/- 1.11
40ºC/75%RH			8.21 +/- 1.02	6.73 +/- 0.85

Average weight gain for 3M stability samples of encapsulated beads in HDPE bottles was less than 1% at all ICH conditions.

DISCUSSION

Coated *Echinacea purpurea* beads were produced successfully, and they were protected from moisture absorption by the moisture barrier film coatings. After 18 months storage in PVC containers at room temperature and humidity, the beads coated with either coating system were still free flowing. In contrast, the unprocessed powdered extract liquefied after 3 hours when exposed to the same condition in a glass Petri dish.

The EMC of the extract powder is 32% at 25°C/60%RH, while the coated high drug-loaded beads have an EMC of 24% for each coating. The low drug-loading beads have an EMC of 17.5% and 14% for the 20A29073 and 85G66695 coatings, respectively. According to the classification system proposed by Callahan[3], the extract powder is in Class VI, Very Hygroscopic while the coated beads fall into a lower category Class III, Moderately Hygroscopic. The classification further confirms the significant difference in hygroscopicity characteristic between the powder extract and the film coated beads as well as the bead-in-capsule dosage forms.

CONCLUSIONS

A stable, solid form of *echinacea purpurea* beads was prepared by layering an aqueous extract onto non-pareil beads followed by an application of a moisture barrier film coating of Opadry or Opadry II. The physical stability of the beads was proven satisfactory for up to 18 months as compared to a few hours of the unprocessed powdered extract. Similar stability was also obtained with beads-in-capsules. This technology can also be applied to other hygroscopic herbal extracts and pharmaceutical actives.

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REFERENCES

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2. Visalakshi, N.A. ; Mariappan, T.T ; Bhutani, H. Pharm *Dev and Tech* **10**. 498-497 2005.
3. Callahan, J.C. et al *Drug Dev Ind Pharm.* **8**. 355-369 1982.

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