

Taiwan's case : American Ginseng (*Radix Panacis Quinquefolii*)

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Outline

- **PDC-339 as an example**
- **Control of Raw Material**
- **Preparation of Substance and Product**
- **Specification of PDC-339**
- **Scope of PDC-339 products**

PDC-339 as an example

| | SiJunZiTang (四君子湯 ; four mild drugs decoction)* | | | |
|------------------------------|---|-------------------------------|---------------------------|--|
| | Ginseng Radix (人蔘) | Atractylodis Rhizoma (白朮) | Poria (茯苓) | Glycyrrhizae Radix (甘草) |
| 君 (The active components) | Radix ● | | | |
| 臣 (Assist) | | ● | | |
| 佐 (Send) | | | ● | |
| 使 (Adjuvant drug) | | | | ● |
| Functions | to benefit digestive system | to modulate the immune system | to eliminate the dampness | to adjust the functions of ingredients |

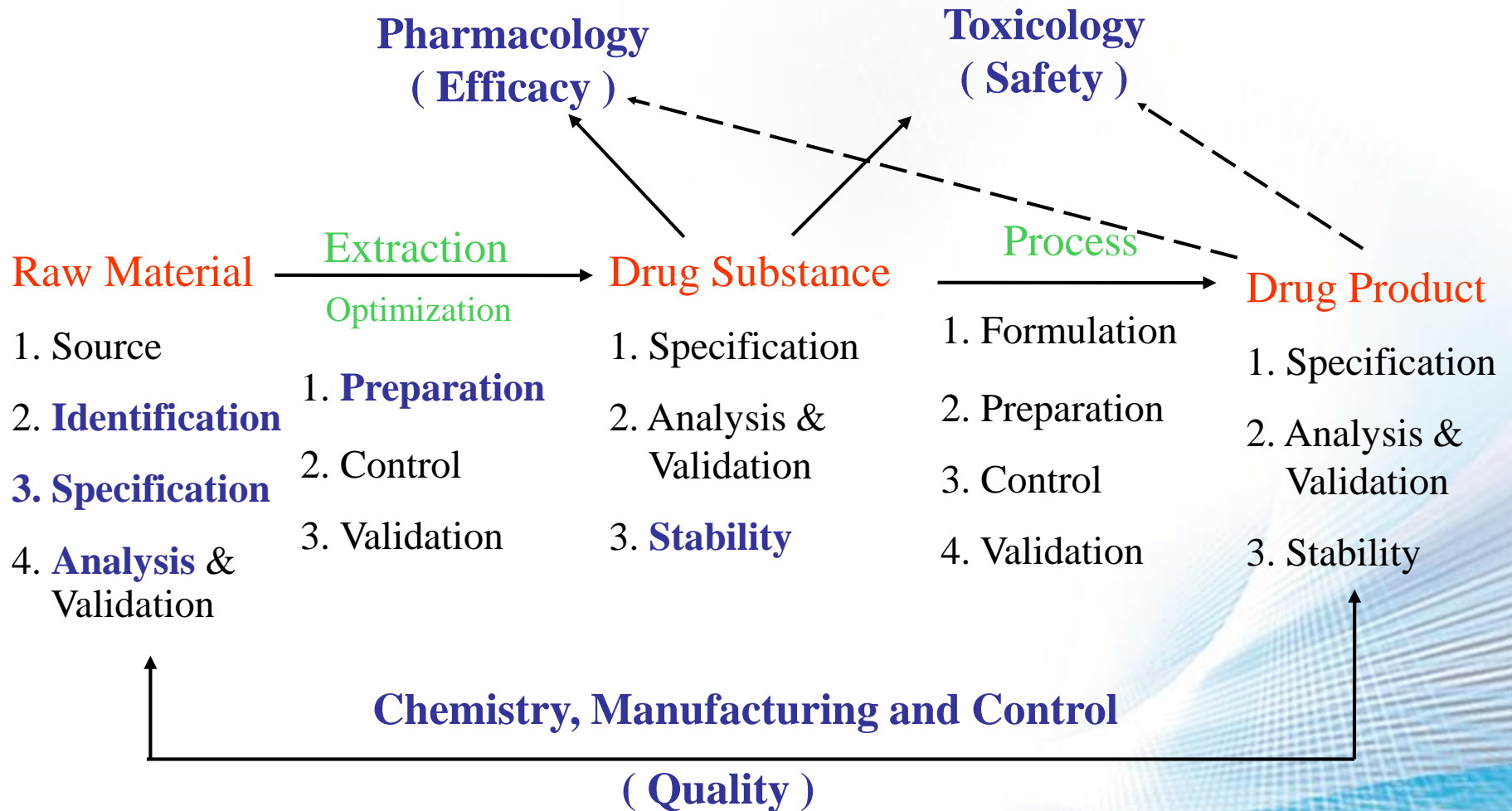
*Prescription of Ancient Son Dynasty (宋朝太平惠民和劑局方)

Strategy: from multiple herbs to single herb

(Ginseng Radix → American Ginseng)

PDC-339 as an example

● Pre-clinical studies



Control of Raw Material

● American Ginseng-Description

- ◆ **Fusiform, cylindrical or conical, 3-20 cm** (occasionally up to 24 cm) **long, 4-28 mm** (occasionally up to 34 mm) **in diameter.**
- ◆ **Externally yellowish-brown, yellowish-white, pale yellowish-brown or pale yellowish-white,** exhibiting transverse annulations and linear lenticels, and showing shallow, fine and dense longitudinal wrinkles, and scars of rootlets.
- ◆ The middle and lower part of the main root, with one to several lateral roots, are mostly broken off. In some cases, the upper end presents remains of a rhizome (**Lutou**), with prominent annular nodes. Stem scars (**Luwan**) rounded or semirounded, with adventitious roots (**Ding**) remaining or already broken off.
- ◆ **Odour slight but characteristic; taste slightly bitter, gradually becoming sweet.**



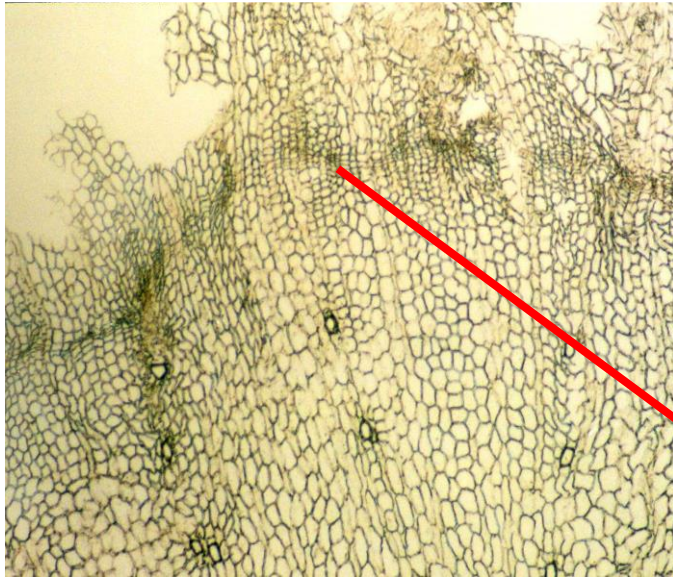
Control of Raw Material

● American Ginseng-Microscopic Identification

- ◆ **Transverse section** Cork consists of 6-8 rows of elongated tangential cells, with several layers often peeled off at the outer side.
- ◆ Resin canals scattered, surrounded by 5-11 secretory cells. In the phloem, resin canals are frequent and usually arranged in 1-3 concentric rings, the rays in the outer part with clefts.
- ◆ **Vessels mainly reticulate and scalariform**, but annular and spiral vessels can also be observed.
- ◆ Cortex consists of more than 10 rows of parenchyma cells, some containing **cluster of calcium oxalate**.
- ◆ Cambium ring distinct. Vessels scattered singly or in groups of 2-10, with interrupted radial arrangement, and lignified or slightly lignified. Rays consist of 1-4 rows of cells wide. Parenchyma cells contain **starch granules**.

Control of Raw Material

● Microscopic Identification

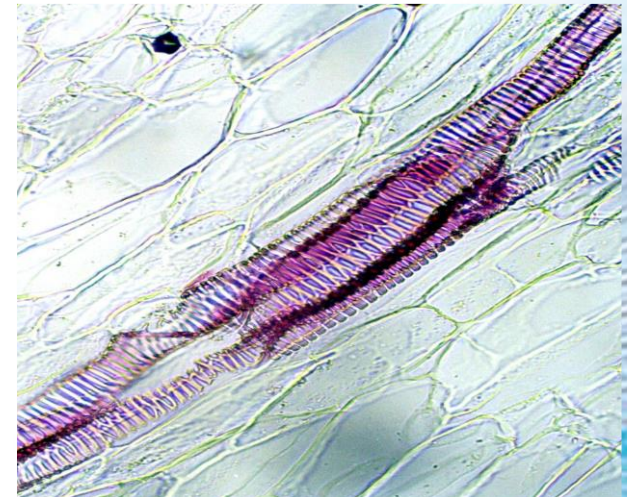


Transverse Section

Cambium



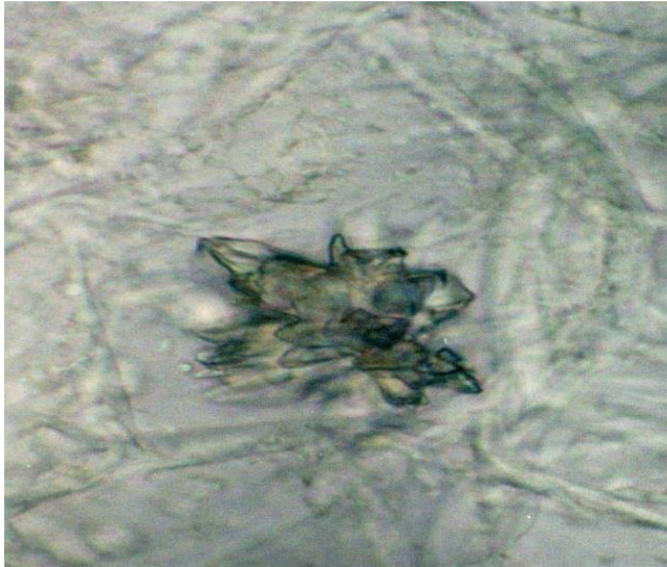
Scalariform Vessel



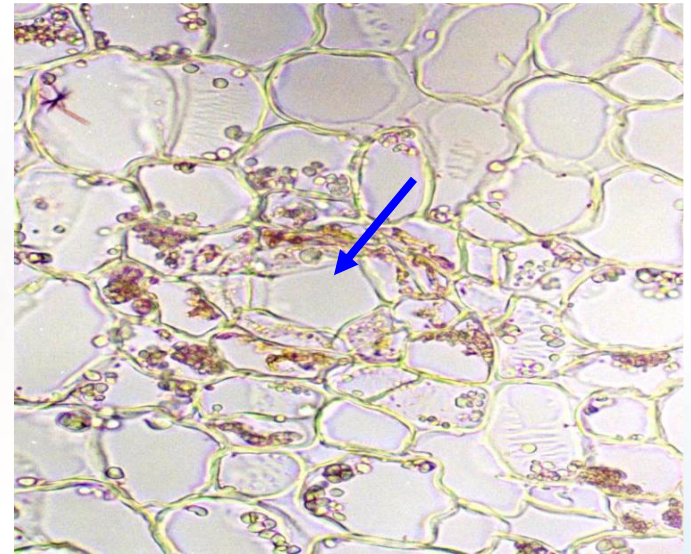
Reticulate Vessel

Control of Raw Material

● Microscopic Identification



Calcium Oxalate Clustered Crystal



Resin Canal



Starch Grain

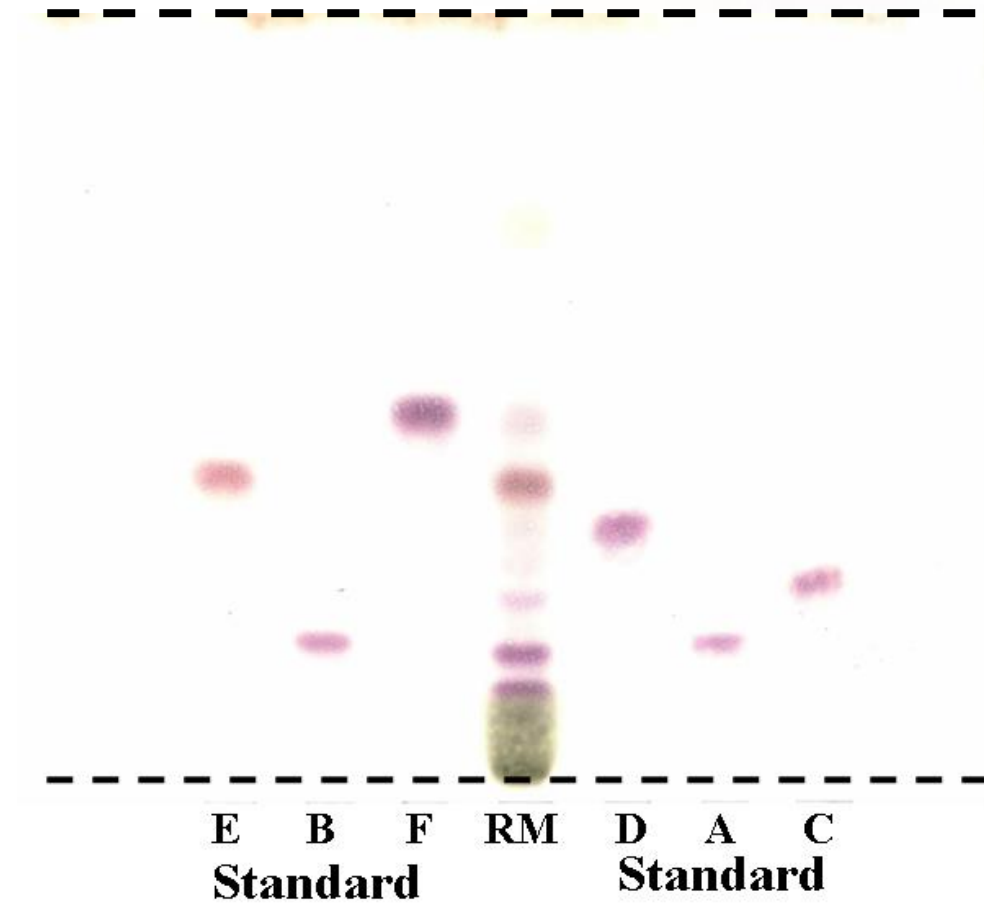
Control of Raw Material

● Specification of RM

| Test Item | Acceptance Criteria |
|----------------------------------|---|
| Botanical Characteristics | Transverse section shown light brown circular rings around cambium with scalariform, reticulated vessels ; reddish brown resin material around epidermis and core ; abundant of oxalic acid calcium crystals spread around epidermis and core. Possesses unique odor. |
| Identifications | TLC Same <i>R_f</i> value as reference standards for A, B, C, D, E and F. |
| Assay | HPLC, A quantity of A, C, D and E. A mg/g ; C NLT mg/g ; D NLT mg/g ; E NLT mg/g |
| Loss on Drying | Not More Than 13.0% |
| Total Ash | Not More Than 7.0% |
| Acid Insoluble Ash | Not More Than 1.0% |
| Water Extractives | Not Less Than 25.0% |
| Alcohol Extractives | Not Less Than 24.0% |

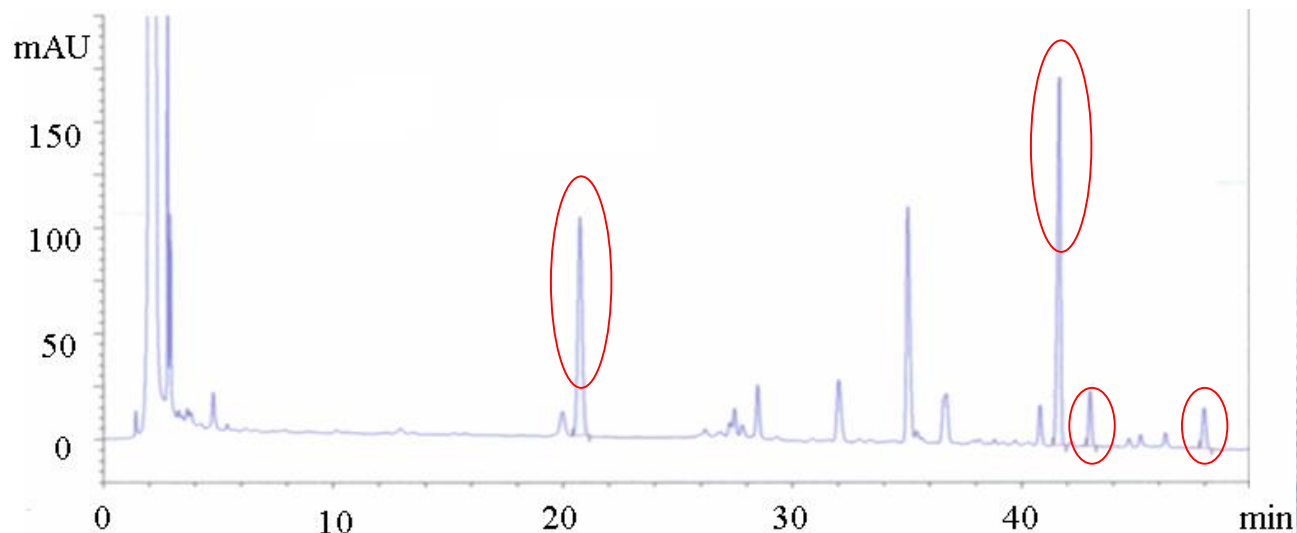
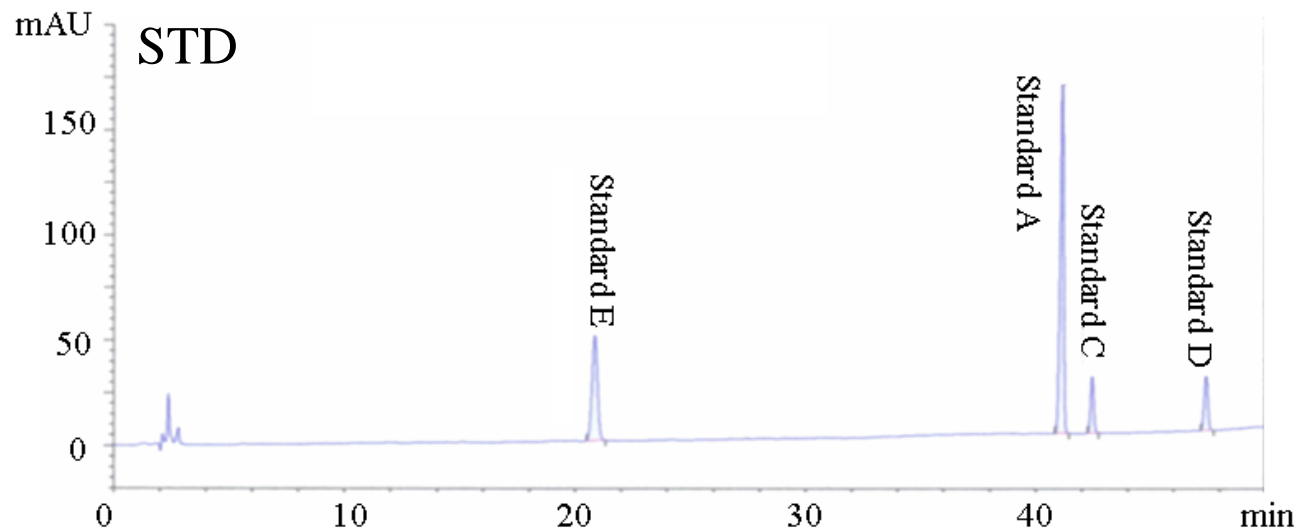
Control of Raw Material

- TLC&STD (Ginsenosides-saponin)



Control of Raw Material

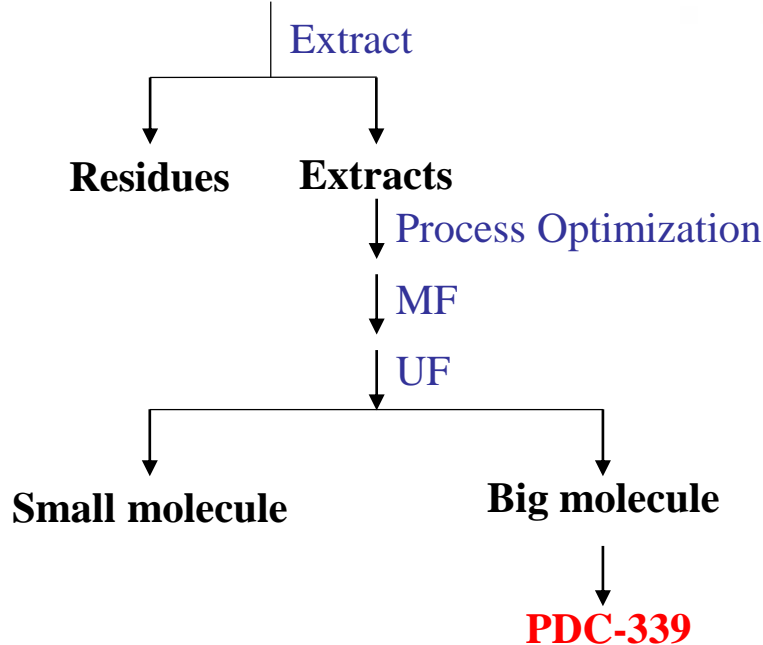
● HPLC



Preparation of Substance and Product

● Preparation

American Ginseng



Validation

In-Process Control

SOP

Raw Material

↓
Extraction (Temperature and time of extraction)

↓
Crude extracts (Solid content rate, Yield)

↓
Steps (Time, Solid content, TLC identification)

↓
Dries (In-process control)

↓
Drug substance (QC analysis)

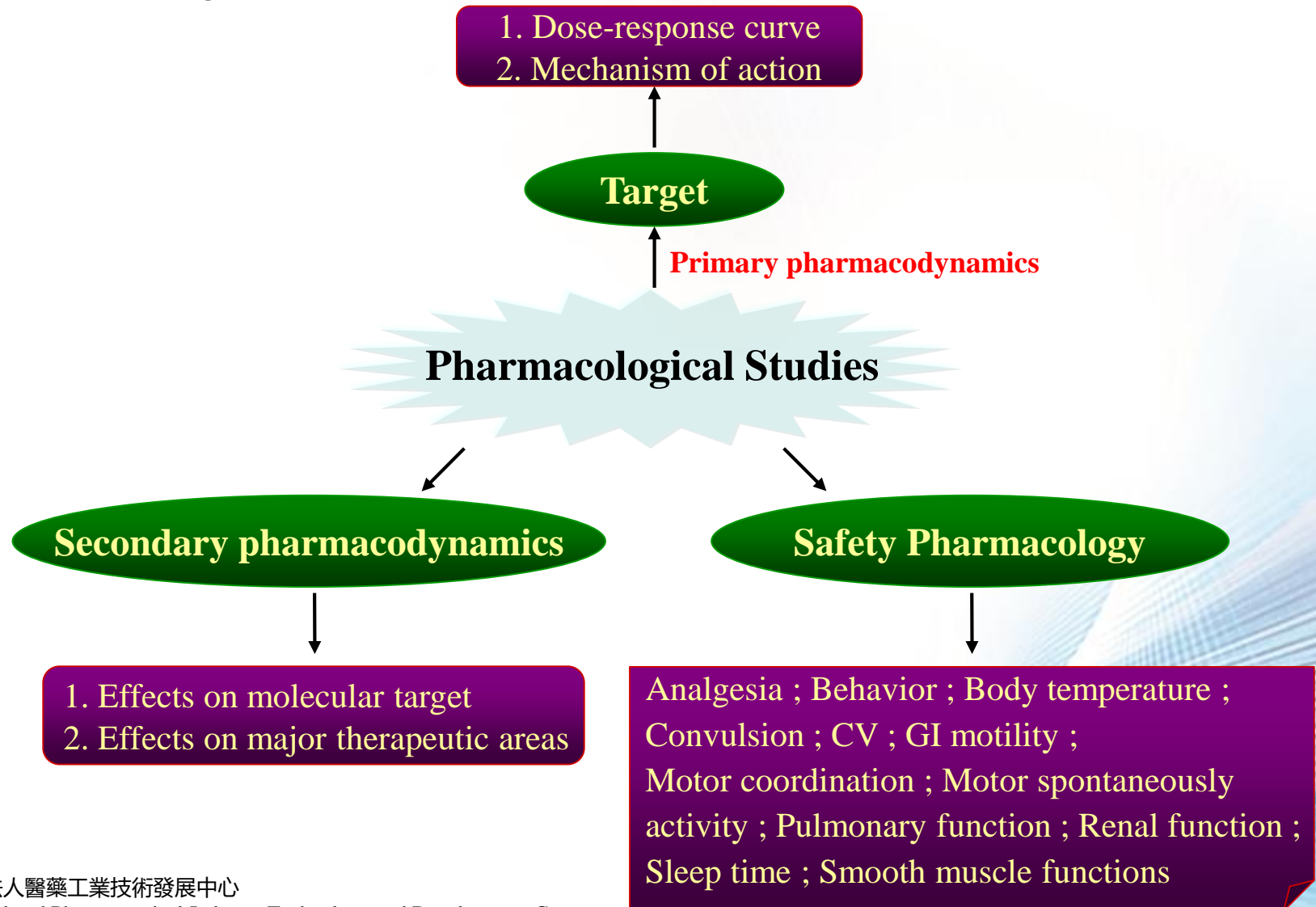
↓
Mix drug substance with excipients

↓
Granulation (In-process control)

↓
Drug product (QC analysis)

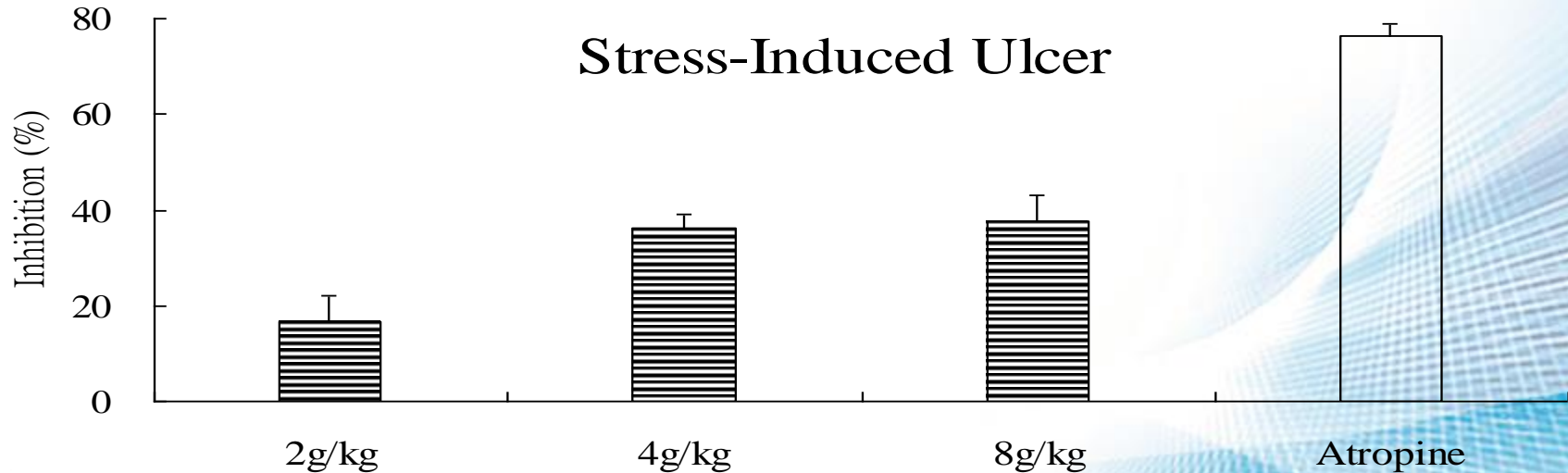
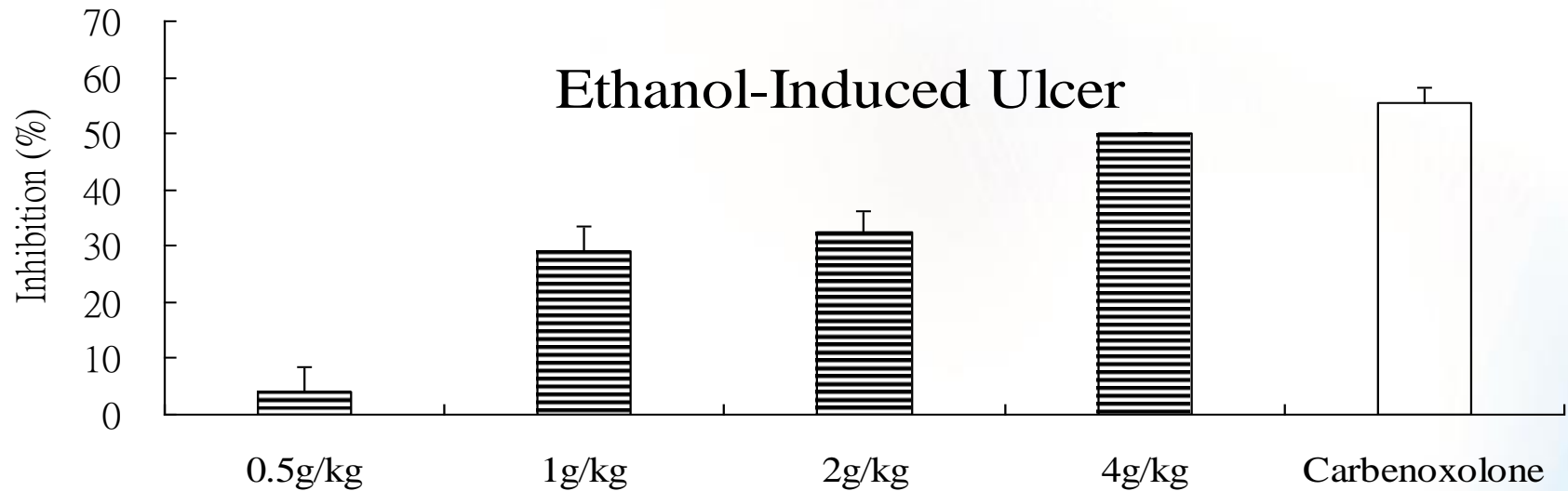
Specification of PDC-339

● Pharmacological Studies



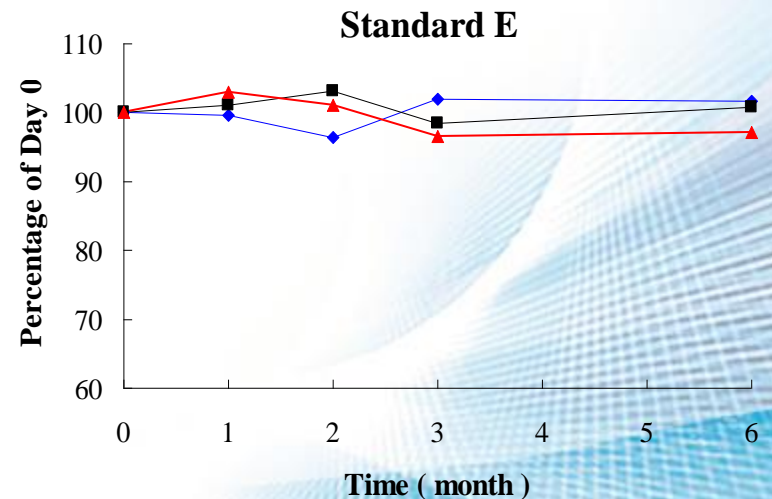
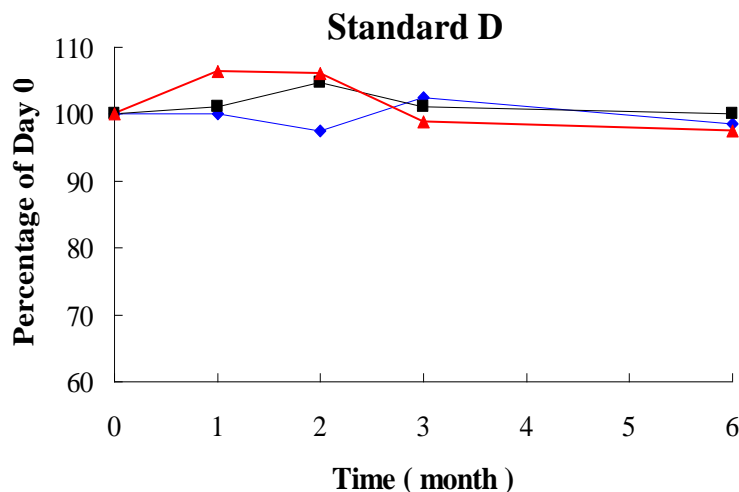
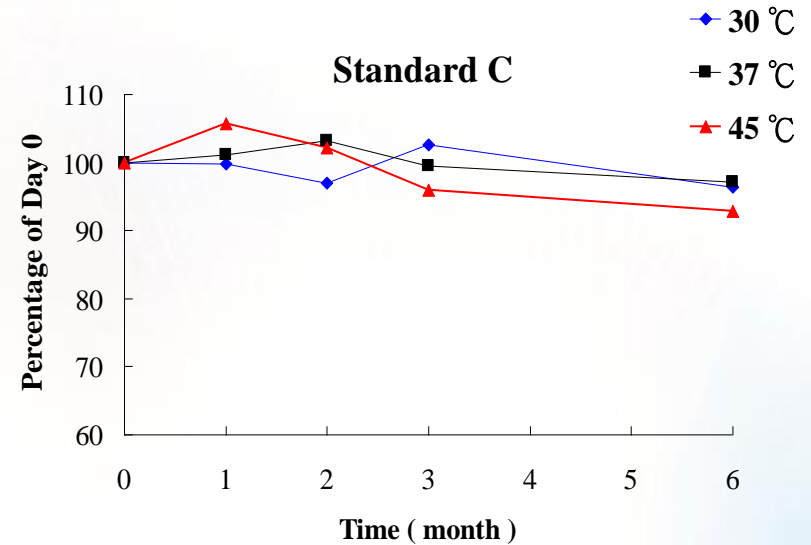
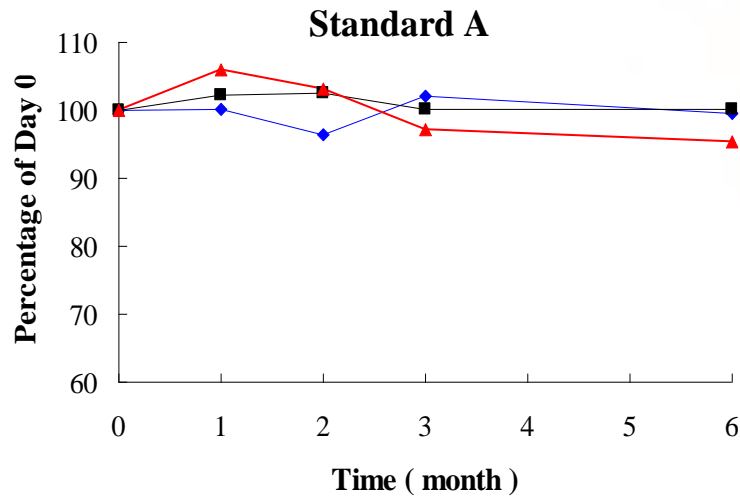
Specification of PDC-339

● Pharmacological Studies



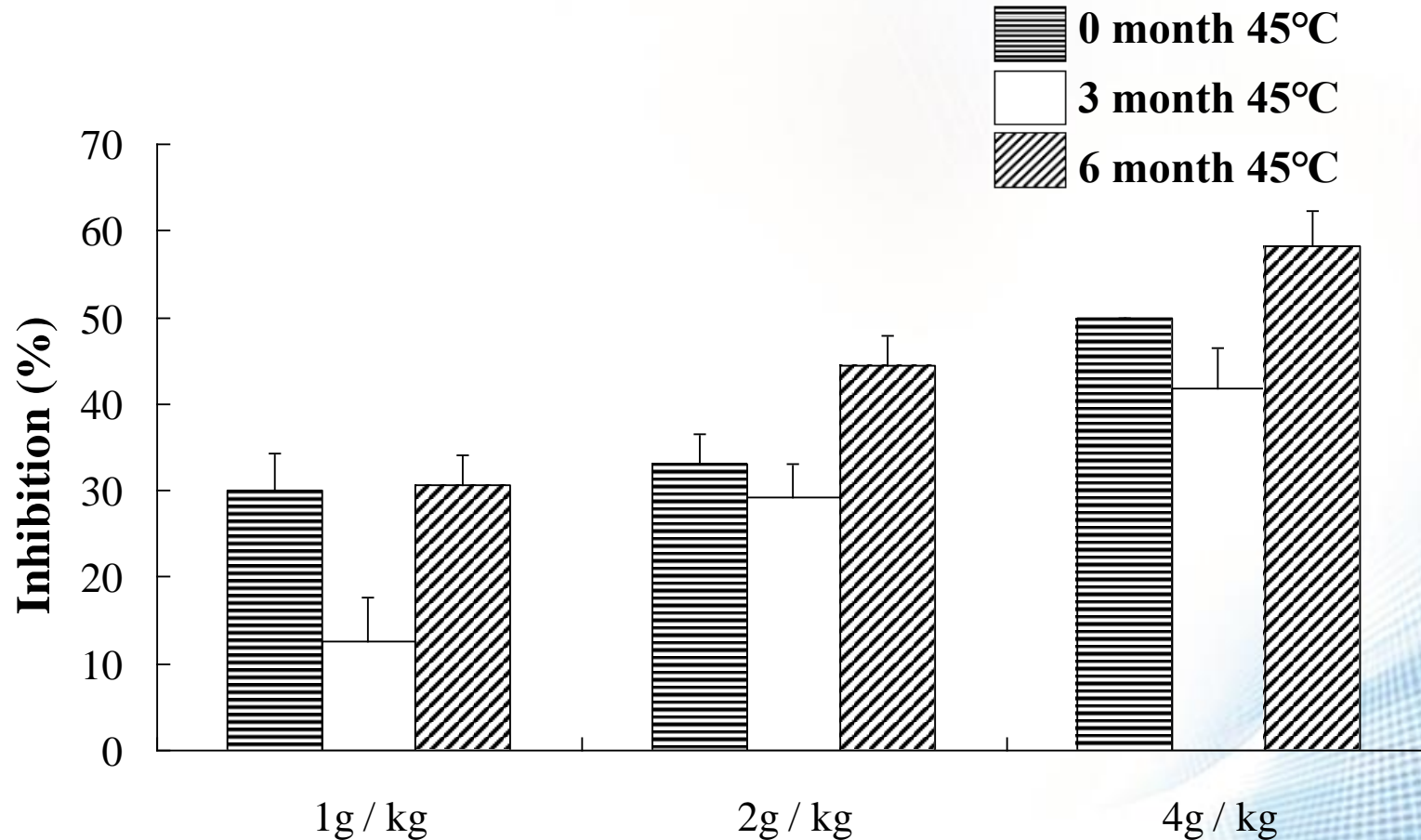
Specification of PDC-339

● Stability Study-Chemical



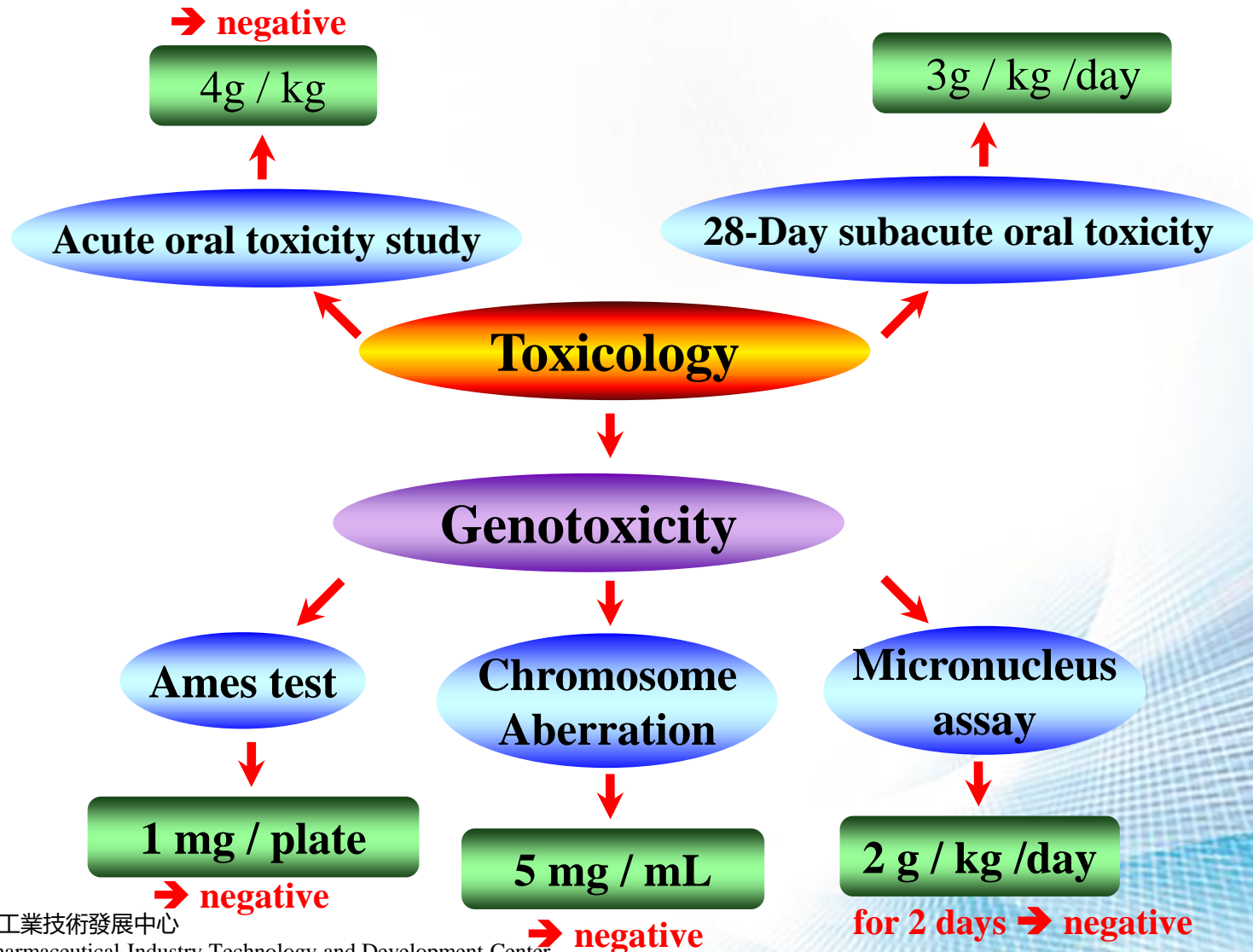
Specification of PDC-339

● Stability Study-Pharmacological (Biological)



Specification of PDC-339

● Toxicology & Genotoxicity



Specification of PDC-339

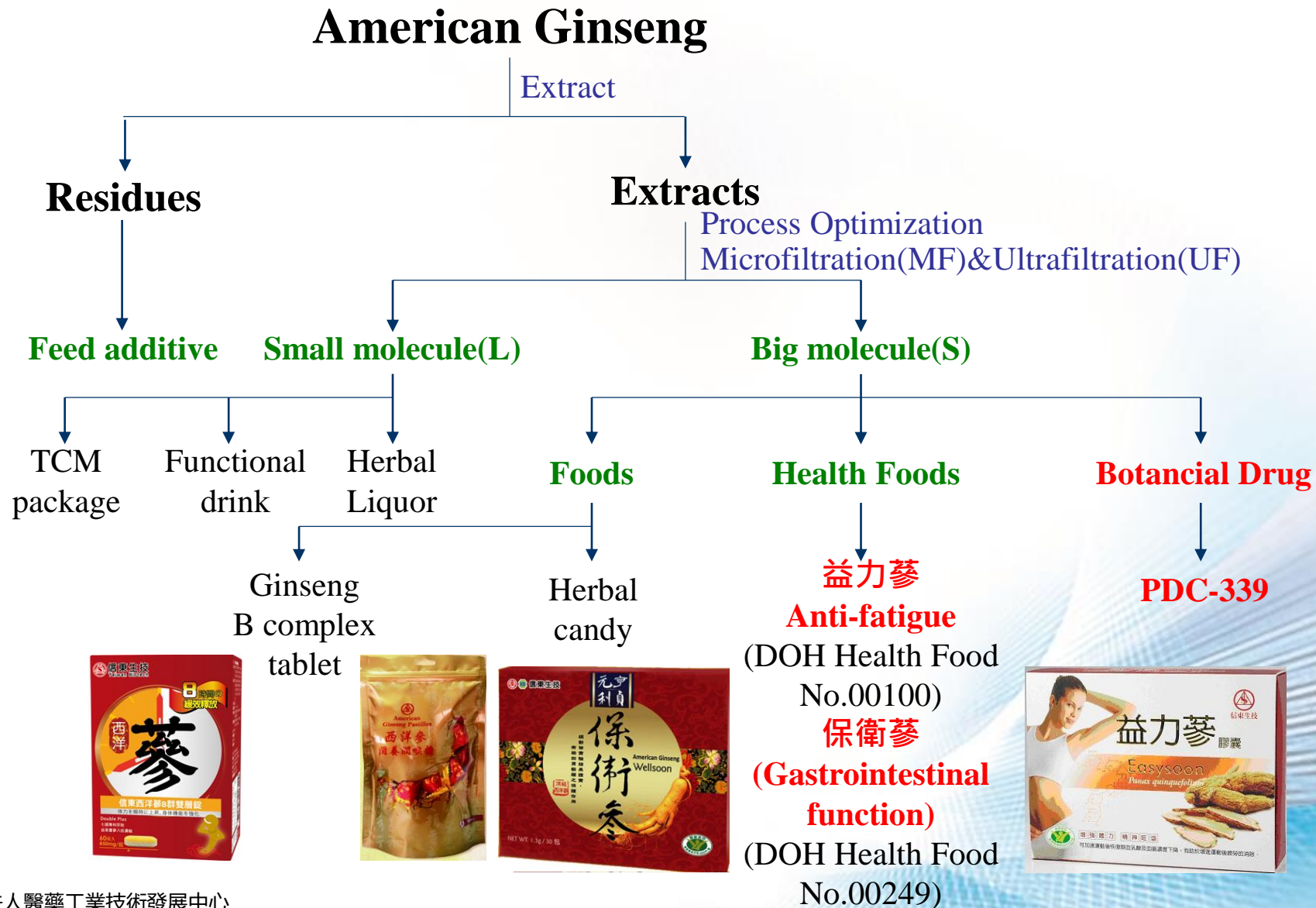
● 28-Day Subacute Oral Toxicity Study-Conclusion

The results of this 28-day oral toxicity study of PDC-339 in rats did not indicate any significant drug treatment related differences in mortality, clinical signs, body weights, total body weight gains, food consumption, ophthalmologic examination, urinalysis, hematology, serum chemistry, organ weights, organ to brain weight ratio, as well as the gross changes between the control, low, medium and high dose groups. In addition, there was no drug treatment related histopathological changes observed among the control and treatment animals in this study. Nasal hemorrhage and corresponding histopathological lesions in lung were observed in one control male rat, these findings were believed to be associated with dosing accident.

In conclusion, the results of this study suggest that PDC-339 did not induce any observable adverse effects in SD rats dosed orally with dose level up to 3000 mg/kg/day for 28 days. Therefore, the 28-day NOAEL for rats ingesting PDC-339 is determined to be greater than 3000 mg/kg/day.

The information generated from this subacute toxicity study can be used for extrapolating a safety margin dose for human consumption of PDC-339.

Scope of PDC-339 products



THANK YOU FOR YOUR ATTENTION!!

