

1 General points

- **Select the longest part of text describing a single idea.** For example, if two drugs are cited as follows 'Warfarin and heparin', the two drugs should be selected separately, with the 'and' in between. But if text is 'Warfarin, an anticoagulant', this whole part of sentence should be selected at once since 'anticoagulant' refers to warfarin, it is therefore a single idea.
- **The annotation should be independent of the context.** For example, if you see an interval of time, you should always annotate it as a 'duration', even if it doesn't relate to a treatment duration.
- **If the punctuation is outside or at the ends of a text bloc** (for example, the name of the drug is in parentheses, or there is a dot right after an idea), **the punctuation should not be selected as part of the class.**

2 Doccano

To annotate the texts, you will have to use Doccano. Doccano is a free annotation tool available at <https://github.com/doccano/doccano>. Full informations about how to setup the tool are available there. To summarize:

- **If it is the first time you use Doccano on your computer**, use the following command to initialize the tool:

```
doccano init
```

- **Always assuming you are using Doccano for the first time on your machine**, setup your account using:

```
doccano createuser --username admin --password pass
```

Your login is now 'admin' and your password 'pass'. You can change it by changing the corresponding values in the command, but it is not important as nobody will have access to your instance of the tool anyway.

- **Start the server:**

```
doccano webserver --port 8000
```

You can now access the tool on any browser by using the following address: 127.0.0.1:8000 or localhost:8000

- **Whenever you want to upload or download texts or labels from a file, start a second terminal and use the following command:**

```
doccano task
```

Without that command, your upload/download form the Doccano interface will never end. To upload a new set of text to annotate it, open your project, go to 'dataset', select 'actions' and then 'upload'. To extract the file containing your annotations, use the same process but select 'export dataset'. You can upload new texts in an existing project, they will simply add up at the end of the existing ones. The process is the same for importing/exporting labels.

- Once you are done with the annotation, close doccano. To do so, go on your terminals where 'doccano task' and 'doccano webserver' are running, and type 'Ctrl' and 'c' at the same time.

3 Classes

3.1 Drug

Entities describing a chemical active compound excluding those with natural origin. Drugs can be described by their INN, commercial name, therapeutic class or IUPAC name.

- Upon anamnesis, it was found that he had been receiving **simvastatin** 40mg daily (every night) since October 2008 for hypercholesterolaemia and oral **linagliptin** 5mg daily since September 2017 for type II diabetes mellitus along with other concomitant medications. 1
- The control group was treated with only **warfarin** without any additional herbal remedy during the clinical trial. 2
- The prescribed **warfarin (3-(-acetonylbenzyl)-4-hydroxy-coumarin)** drugs were **Warfar®** (2 mg/tablet, Korea United Pharm., Inc., Seoul, Republic of Korea) and **Coumadin®** (5 mg/tablet, Jeil Pharm.), which is a racemic mixture composed of equal amounts of 2 optical isomers. 2
- This open-label, fixed-sequence study enrolled 15 HIV-infected patients who had been receiving **antiretroviral therapy with etravirine** (400 mg once daily) for at least 4 weeks and whose HIV-1 RNA load in plasma was ≤ 50 copies/ml.

3.2 Herbal product

Herbal products relates to entities describing an herbal product.

3.2.1 Herb name

Denomination of the herb, either in their vernacular or binomial form. They also include molecules and commercial name of products of herbal origin

- Additionally, he was also consuming multiple vitamins and herbal supplements which included oral **stevia [Stevia rebaudiana]** for 2–3 months. 1
- The **ginseng** group was given **P. ginseng** (aqueous extracts 0.5 g) 3 times (10:00/15:00/20:00) a day for 2 weeks in addition to warfarin. 2
- Catechins in **green tea** include **epicatechin**, **epigallocatechin (EGC)**, **epicatechin-3-gallate (ECG)** and **epigallocatechin-3-gallate (EGCG)**,⁸ of which **EGCG** is the most abundant and biologically active. 3
- **EGCG** was administered as two capsules of **Teavigo™**, a commercially available, caffeine-free, 94% pure crystalline **EGCG** (Healthy Origins, Pittsburgh, PA, USA). 3

3.2.2 Herb part

Herb part describes which part of the herb is used.

- The **root** of P. ginseng C.A. Meyer grown for 4 years was obtained from the Department of Pharmaceutical Preparation of Korean Medicine, Korean Medical Hospital, Kyung Hee University (Seoul, Republic of Korea). 2

3.2.3 Extraction process

Type of preparation used to make a complement out of the herb.

- The ginseng group was given P. ginseng (**aqueous extracts** 0.5 g) 3 times (10:00/15:00/20:00) a day for 2 weeks in addition to warfarin. 2
- Freshly **concentrated pineapple juice** was prepared. 4

3.3 Amount

Dosology of either an herb or a drug, or value of a parameter.

- Upon anamnesis, it was found that he had been receiving simvastatin **40mg** daily (every night) since October 2008 for hypercholesterolaemia and oral linagliptin **5 mg** daily since September 2017 for type II diabetes mellitus along with other concomitant medications. 1
- All patients were scheduled to take warfarin at a dosage of one **2mg** tablet per day for the first 7 days and one **5mg** tablet per day for the next 7 days, because of warfarin's half-life and narrow therapeutic index. 2

3.4 Frequency

Any frequency, whatever the context.

- The ginseng group was given P. ginseng (aqueous extracts 0.5 g) **3 times (10:00/15:00/20:00) a day** for 2 weeks in addition to warfarin. 2
- Participants in Arm I and Arm II received a **single oral dose** of celecoxib (100 mg) or montelukast (10 mg), respectively, after pretreatment with 250 ml of either pineapple juice or water (control) for four consecutive days before the beginning of the study. 4

3.5 Duration

Duration of a treatment or intervention, duration of a symptom or hospitalisation required by this symptom, or any other type of duration.

- The ginseng group was given P. ginseng (aqueous extracts 0.5 g) 3 times (10:00/15:00/20:00) a day **for 2 weeks** in addition to warfarin. 2

- finally, EGCG was given **for 10 days** as pretreatment, and then rosuvastatin and EGCG were given concomitantly. 3
- The man was hospitalised for unsteady gait and lower limb weakness **for 10 days** since early August 2018. 1

3.6 Pathology

Pathology describes a medical status of a patient. This entity includes symptomes related to the intervention as well as chronic diseases or medical background and description of absence of pathology.

- The man was hospitalised for **unsteady gait** and **lower limb weakness** for 10 days since early August 2018. 1
- All the patients were monitored for **bleeding** or **adverse effects** that might be related to the study medication
- He had a history of **hypercholesterolaemia**, **stage IIIB chronic kidney disease** and **type II diabetes mellitus**. 1
- Physical examination showed **proximal muscle weakness** of both lower limbs. 1
- This study included **healthy** Korean male or female volunteers aged 20–55 years. 3
- This open-label, fixed-sequence study enrolled 15 **HIV-infected** patients who had been receiving antiretroviral therapy with etravirine (400 mg once daily) for at least 4 weeks and whose HIV-1 RNA load in plasma was 50 copies/ml. 5

3.7 Parameters

Parameters relate to observable biological events giving indications on patient status. Can be a physiological, pharmacokinetic, ... Only includes parameters relating to human physiological status.

- During hospitalisation, his **serum creatine kinase (CK)**, **lactate dehydrogenase** and **alanine transferase** were markedly increased. 1
- Warfarin acts by inhibiting the **vitamin K epoxide reductase** which is needed to activate **vitamin-K dependent coagulation factors**.
- By stratified block randomization based on age, gender, **body–mass index (BMI)**.
- On admission, there was deterioration in **creatinine** 158 µmol/L and renal function from **plasma urea** 13.3 mmol/L two months before, to 256 µmol/L and 24.3 mmol/L, respectively. 1
- In the RMANOVA exploring the relationships among **PT** and **INR** changes, warfarin dose, and ginseng administration, **PT** and **INR** values were both significantly related to warfarin dose (**PT**: p 0.001; **INR** : p 0.001), although there were no significant effects of ginseng (PT: p 0.430; INR: p 0.286). 2

- Given that the **IC₅₀** value of EGCG on OATP2B1 inhibition was 101 μ M (46.30 mg/L) 9 and the **C_{max}** after oral administration of EGCG 200 mg was 73.7 ± 25.3 mg/L, 26 a smaller amount of EGCG could have effectively inhibited OATP2B1. 3
- The PT **AUC** values during the second set of 7 days increased in both the ginseng ($p < 0.001$) and control group ($p < 0.001$) compared to the values during the first 7 days. 2
- There was no significant difference in **T_{max}** between rosuvastatin–EGCG and rosuvastatin alone on Day 4. 3
- Given that the **IC₅₀** value of EGCG on OATP2B1 inhibition was 101 μ M (46.30 mg/L) 9 and the **C_{max}** after oral administration of EGCG 200 mg was 73.7 ± 25.3 mg/L, 26 a smaller amount of EGCG could have effectively inhibited OATP2B1. 3
- The co-administration of pineapple juice with celecoxib significantly improved its **bioavailability** by approximately 160%. 4

3.8 Target

Enzyme, transporter or any other element with a biological role being implied in the described event.

- Weak inhibitory effect of stevia on **CYP3A4** activity played an important role in its interaction with simvastatin and linagliptin as he had genetic susceptibility to myopathy [exact duration of treatments to reaction onset not stated]. 1
- Given that the **IC₅₀** value of EGCG on OATP2B1 inhibition was 101 μ M (46.30 mg/L) 9 and the **C_{max}** after oral administration of EGCG 200 mg was 73.7 ± 25.3 mg/L, 26 a smaller amount of EGCG could have effectively inhibited **OATP2B1**.

3.9 Age

- A **69 year old** man developed rhabdomyolysis following concomitant administration of simvastatin and linagliptin with stevia [not all routes and dosages stated]. 1
- This study included healthy Korean male or female volunteers **aged 20–55 years**. 3
- A total of 24 healthy male subjects **aged from 21 to 38 years** (mean 28 years) were enrolled in the study.

3.10 Sex

- A 69 year old **man** developed rhabdomyolysis following concomitant administration of simvastatin and linagliptin with stevia [not all routes and dosages stated]. 1

3.11 Ethnic group

Ethnic group . Only relates origins (even if this origin is not related to a patient), not names of countries, continents, ...

- Twenty-five (25) patients newly diagnosed with ischemic stroke by brain computed tomography or magnetic resonance imaging in the **Korean Medical Hospital**.
- This study included healthy **Korean** male or female volunteers aged 20–55 years. 3

3.12 Study

Design of the study, describing standardisation processes taken during intervention.

- Subjects of **clinical study**
- This study was an **open-label, randomized control trial**. 2
- 34 patients were enrolled in the study and were **randomized to 1 of the 2 study group**
- **Two arms** were included in this research. 4
- For each arm, a **randomized, open-label, two-way crossover study** design with 2-week washout period between treatments was used. 4

3.13 Cohort

Description of composition of the cohorts.

- Of these patients, a total of **34 subjects** were selected according to the warfarin indications of the fourth American College of Chest Physicians Consensus Conference¹⁹ and product labeling for Coumadin® (Jeil Pharm., Inc., Seoul, Republic of Korea). 2
- This left **25 patients** completing the study, 12 of whom had been allocated to the ginseng group and red13 to the control group. 2
- This study enrolled **two male and 11 female volunteers**.