藥學科技(二)　Scifinder & Innovation 報告

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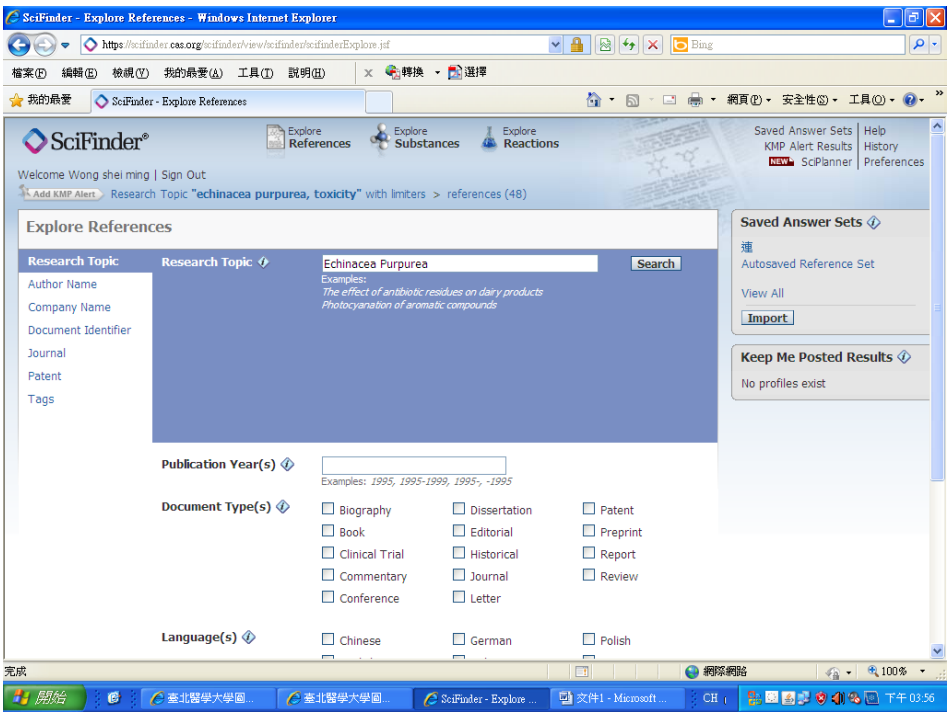
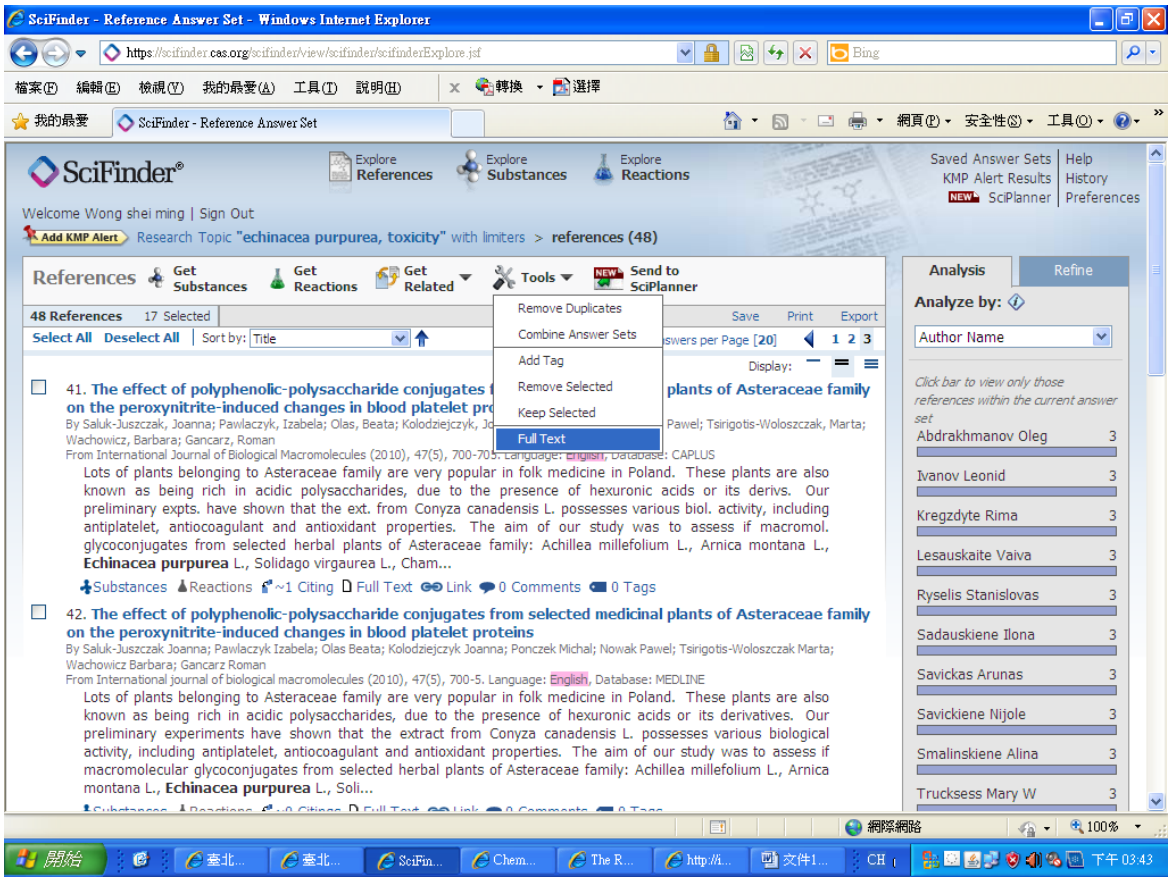
- 主題：紫錐菊 Echinacea Purpurea 天然物簡介及其相關藥理及毒性資料
- **<u>第一部分：Scifinder</u>**
  - 目的：了解並學習如何使用 Scifinder 資料庫。
  - 過程：

1. 登入 Scifinder 後，選擇所要搜尋的資料類別：Explore Refernces，鍵入關鍵字 Echinacea Purpurea。頁面下半欄可選擇搜尋的篩選條件。



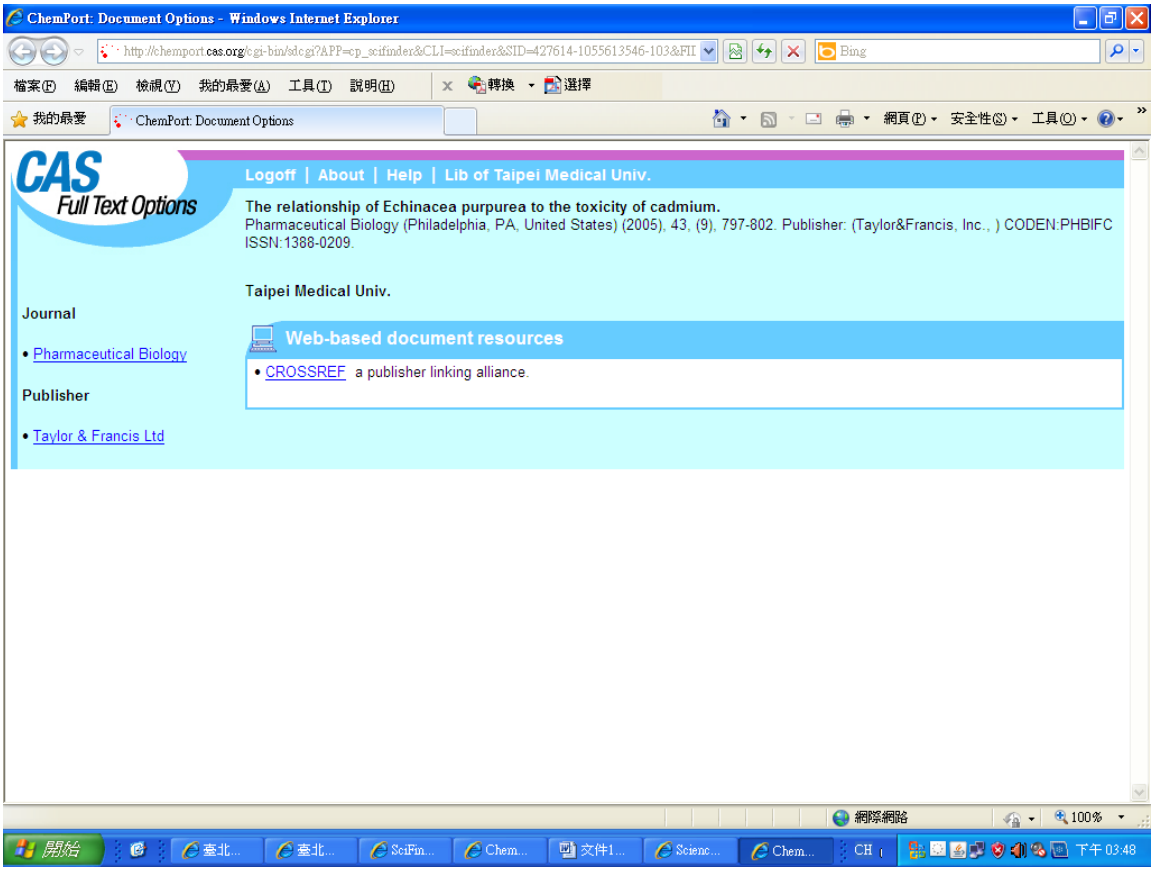
2.搜尋結果條列呈現於頁面，共有 48 筆文獻，文獻中關鍵字會呈現粗體。右手邊則有分析工具，可依喜好的條件篩選所要的資料，例如：作者姓名、論文發表年份等。

3.可勾選所想要閱覽的資料，並選擇上方工具列中的 Tools 鍵中的 Full Text 來瀏覽全文。

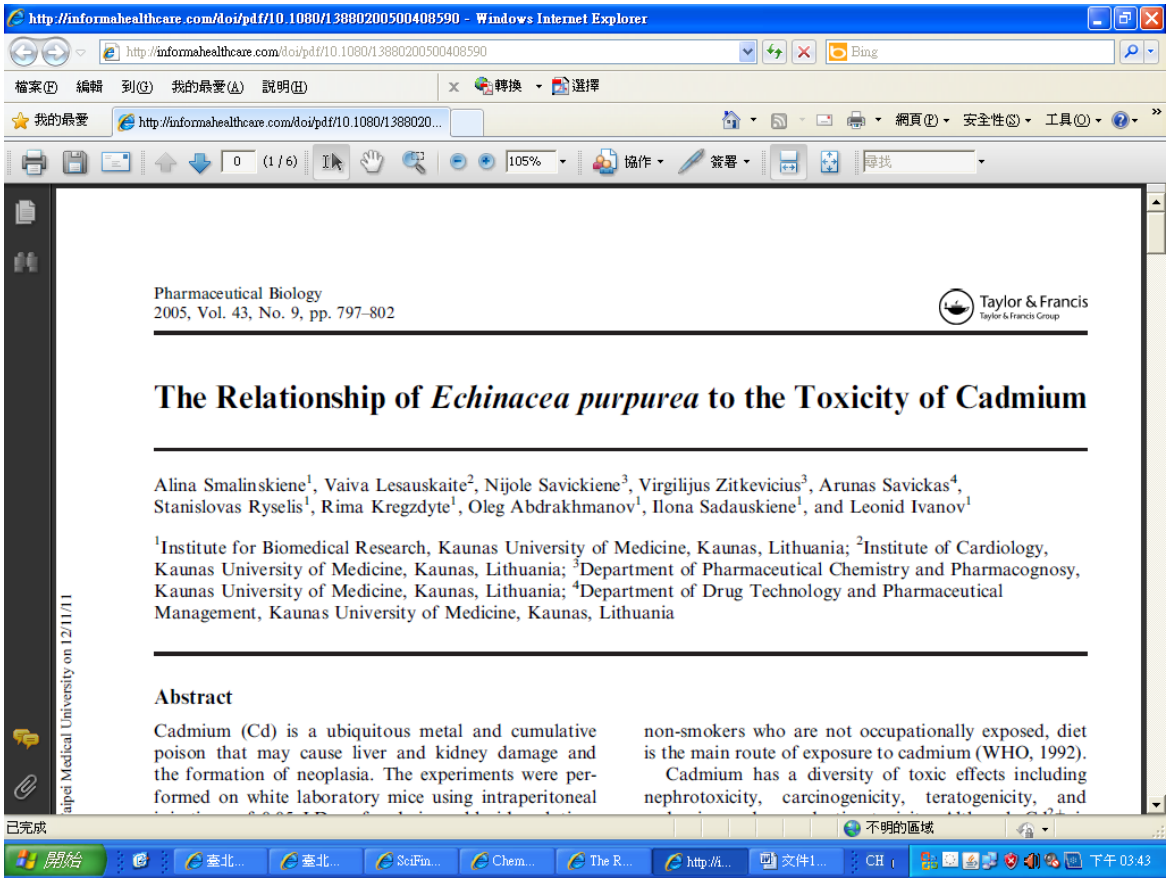


4.所勾選的文獻會列於另一新視窗中，可點擊右方 Full-text Options 來進行資料瀏覽。

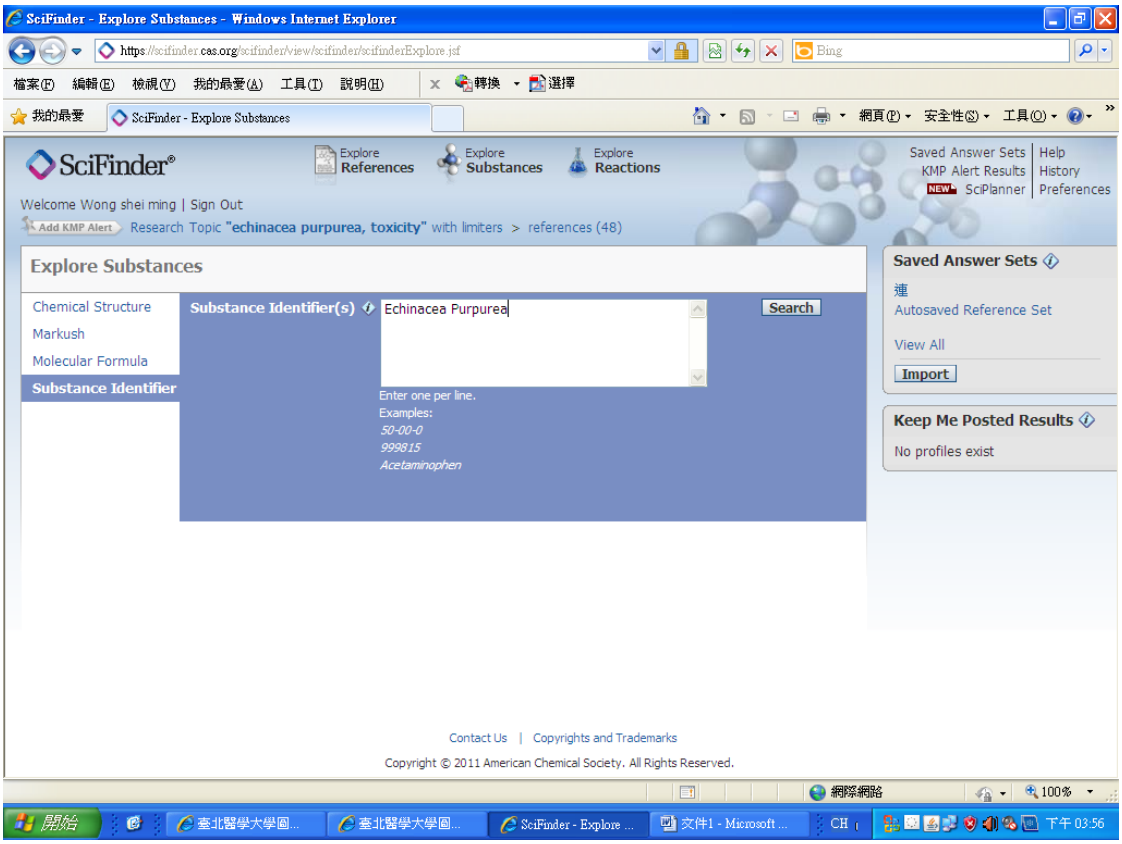
5.點選後再出現另一視窗，可點擊 CROSSREF 連結至資料原網站或開啟資料全文。



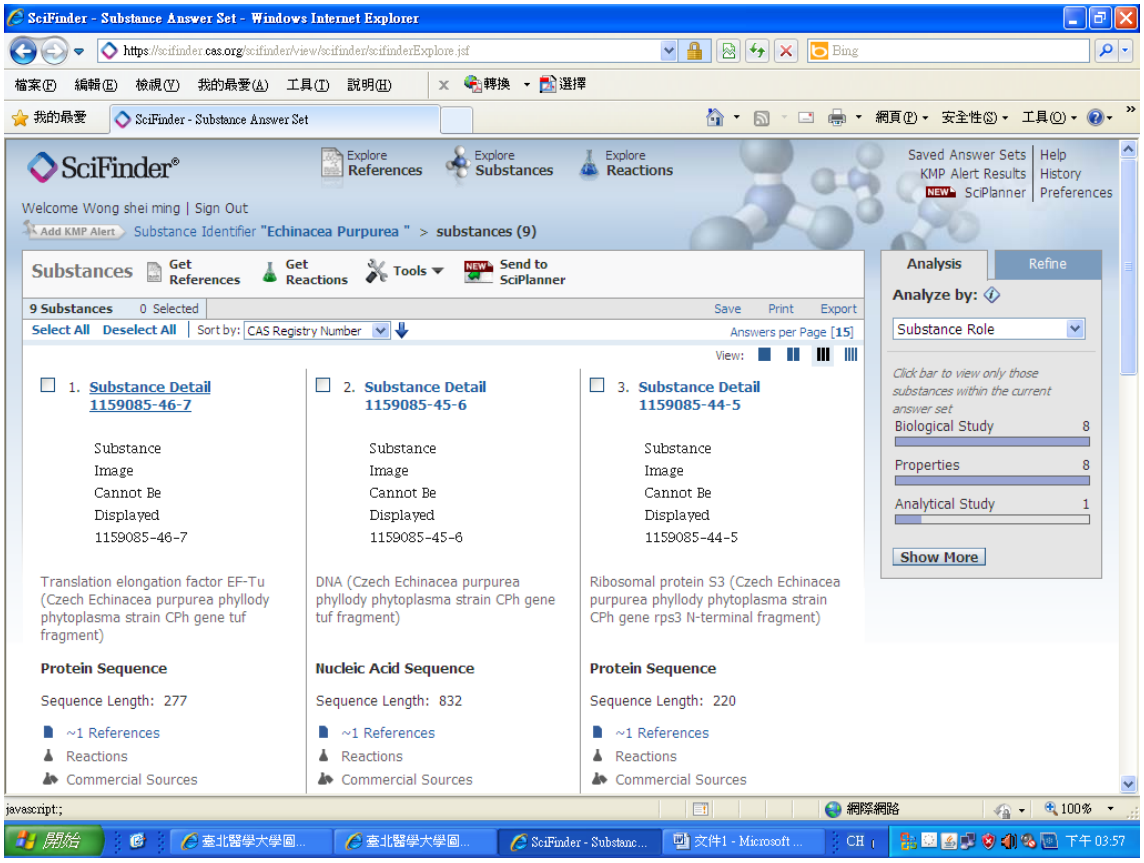
6.取得並開啟文獻 pdf 檔，可另行存檔作為資料參考。



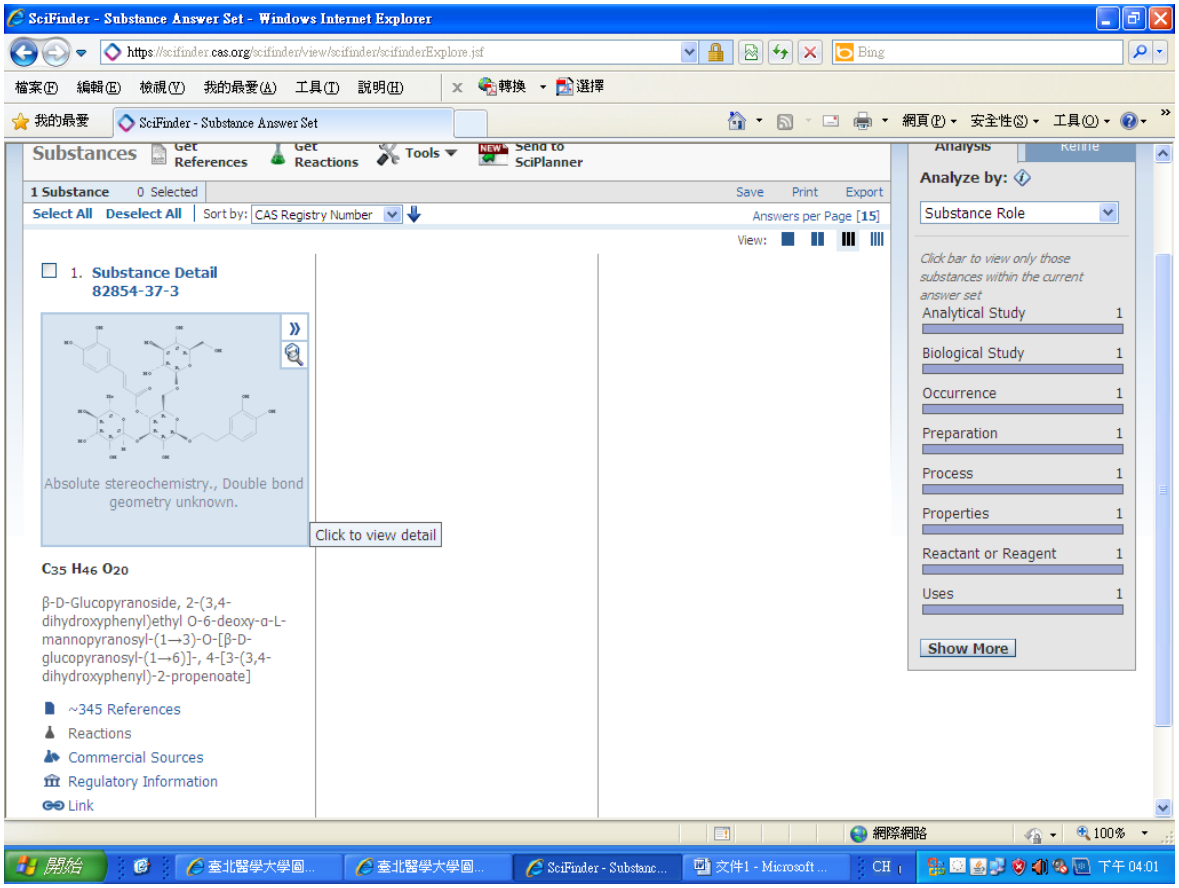
7.再次回到搜尋頁面，點選左列 Substance Identifier，鍵入關鍵字 Echinacea Purpurea。



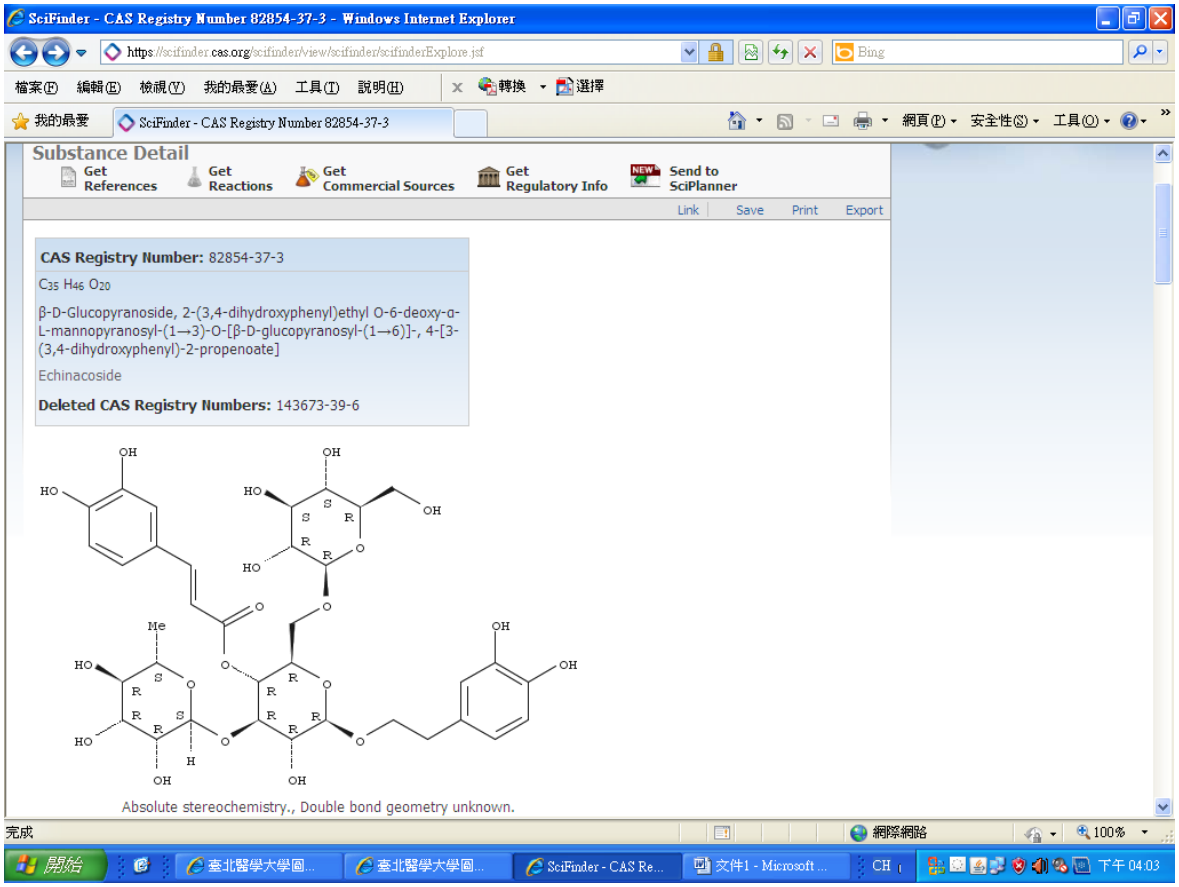
8.找到九筆資料，但是都不是我想要的，後來看到一些資料中說 Echinacea Purpurea 含有一 phenylpropanoid 主要成分 Echinacoside，於是改搜尋之。



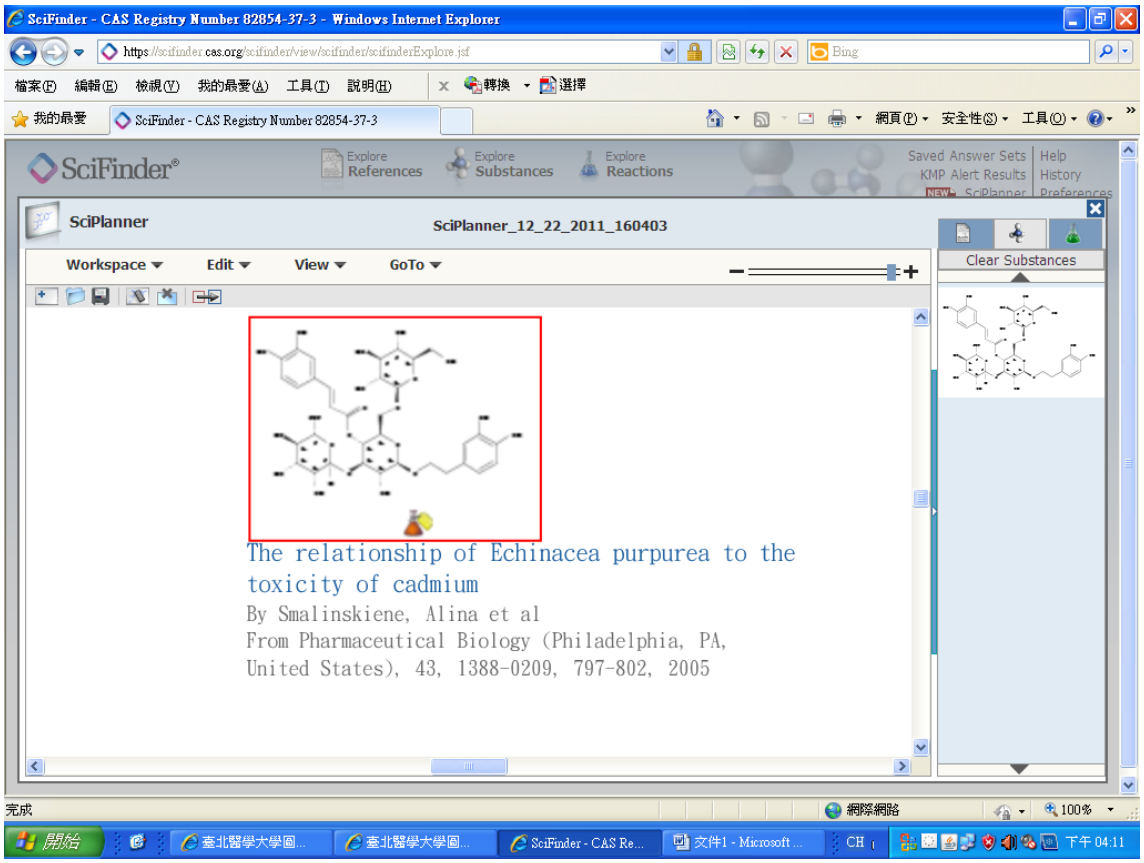
9.搜尋得到其化學結構式，及物質的物化性資料。



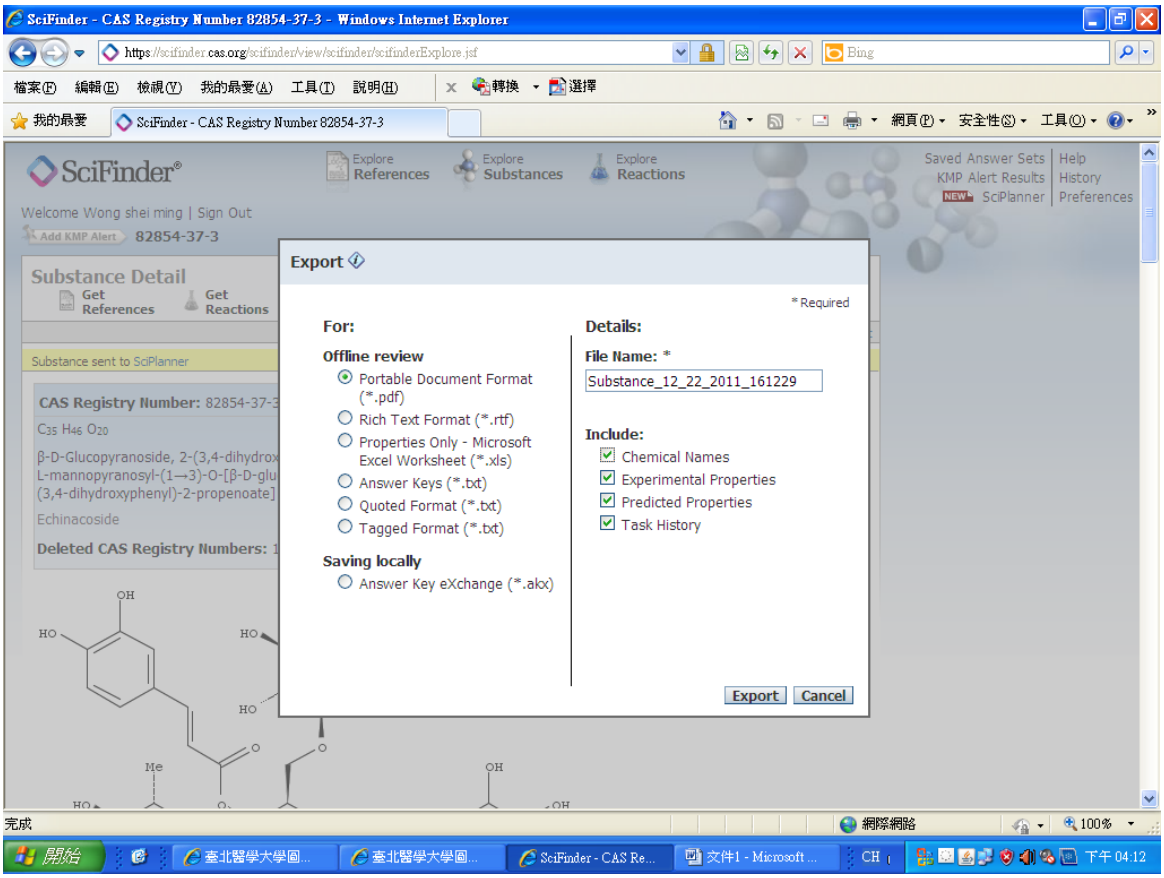
10.點擊開來可見其詳細物質資料。



11.可選擇上方工具列中的 Send to Sciplanner 來儲存並編輯所搜尋得的資料。

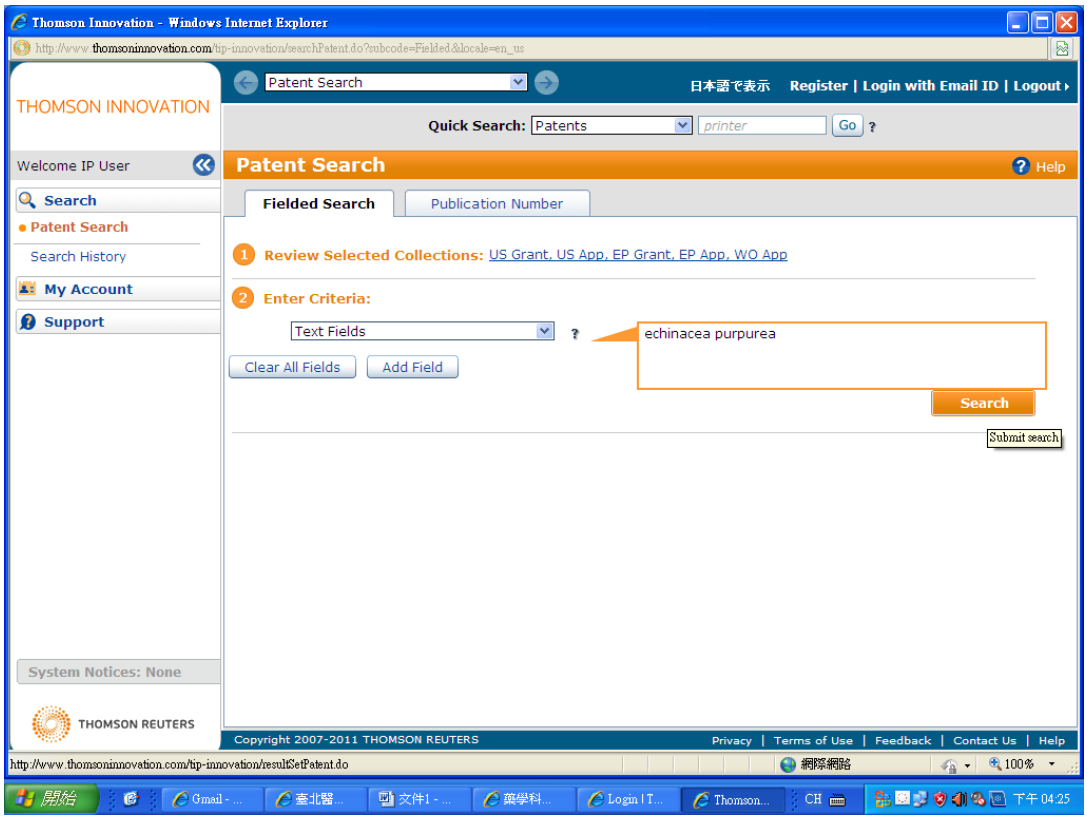


12.編輯好之後可按 Export 鍵輸出，並儲存成想要的檔案類型。

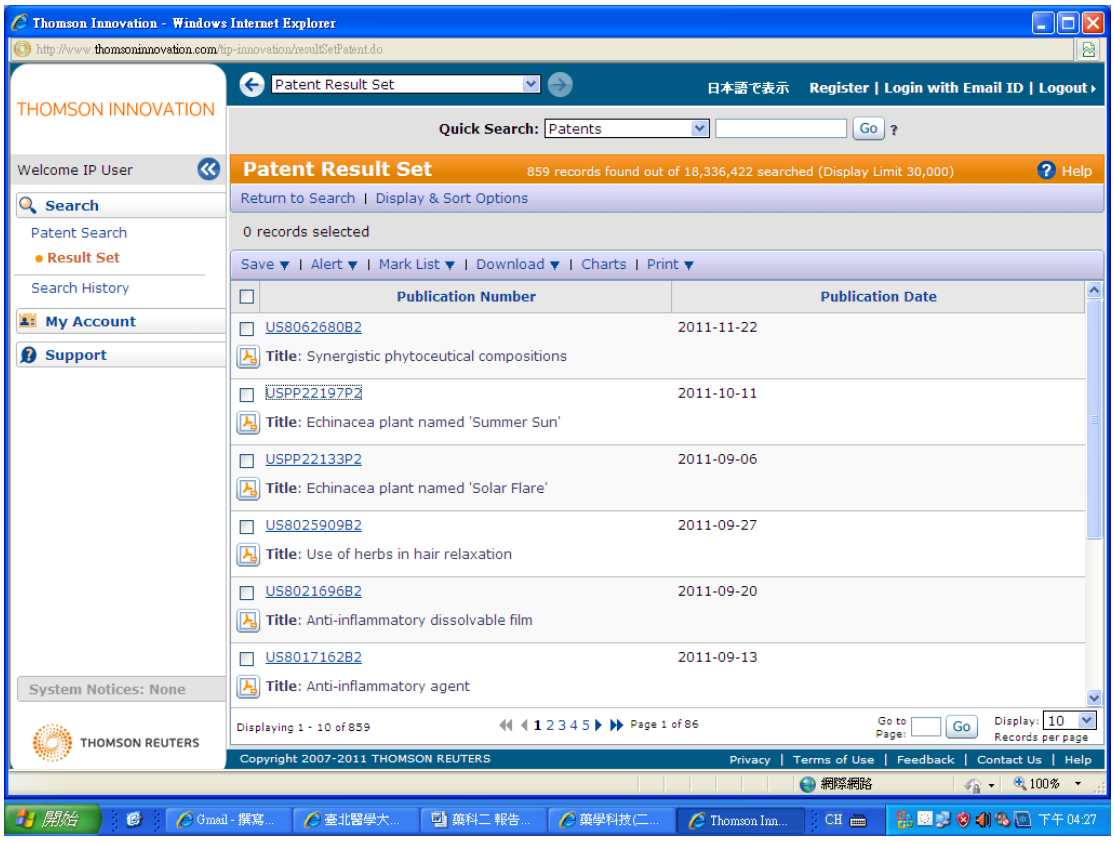


- **第二部分：Innovation 專利檢索平台**
  - 目的：學習如何使用 Innovation 專利檢索平台，並瞭解其應用性。
  - 過程：

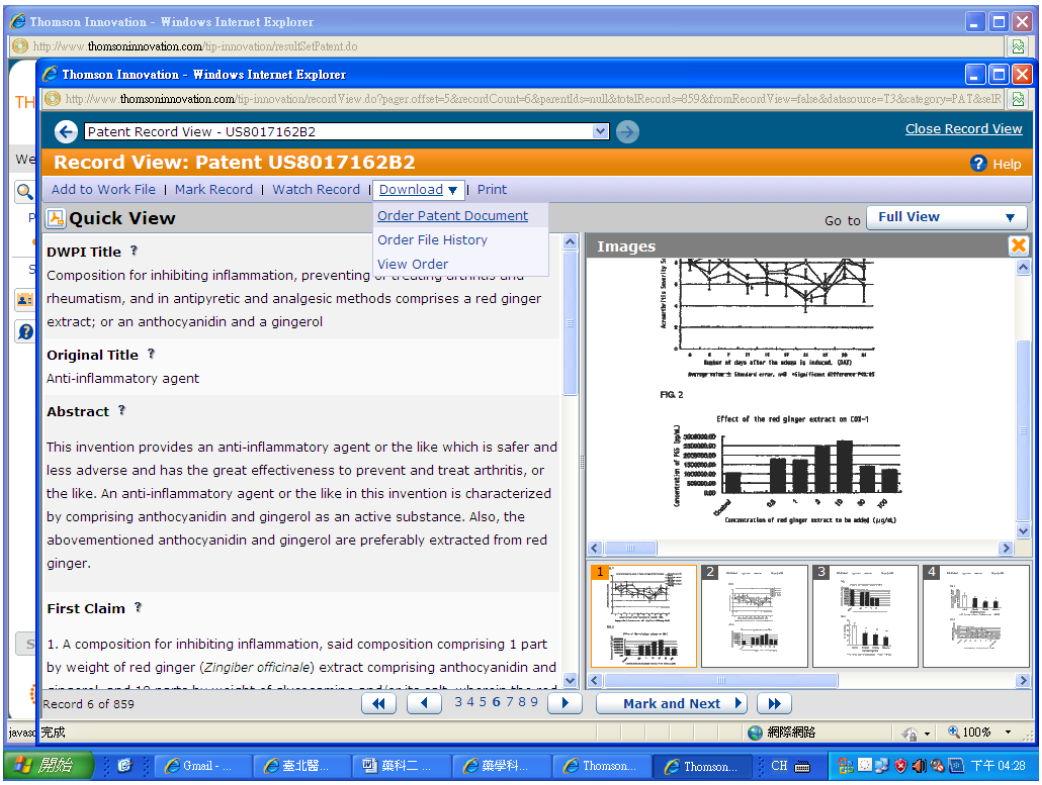
1.登入搜尋頁面，選擇 Fieled Search 進行主題或關鍵字搜索。鍵入 Echinacea Purpurea。



2.搜尋結果以條列方式呈現，可點擊專利編碼來瀏覽專利資料。



3.搜尋到的資料中有許多是不同種 Echinacea Purpurea 的專利資料，也有不同 herbal 抗發炎軟膏劑型的專利。在上方工具欄中可選擇編輯或存檔，但是有些功能因校方沒有購買而無法使用。



- **第三部分：主題報告之整理**
  - 方法：利用前兩部分所搜尋而得的資料整理成簡單主題報告。
  - 內容：

- **Botanical profile**

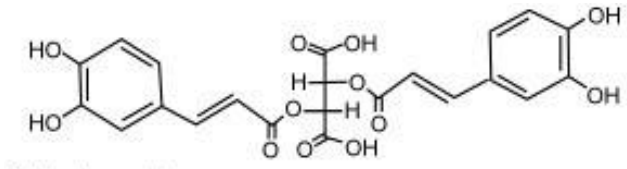
Echinacea Purpurea	
	
Botanical name:	Echinacea
Scientific name:	Echinacea Purpurea (L.) Muench
Family:	Asteraceae
Common names:	Purple coneflower, black Sampson, niggerhead, rudbeckia, hedgehog, red sunflower, snakeroot, scurvy root, Indian head, comb flower, black Susans.

Place of origin:	North America
Brief description:	Echinacea has been used as an herbal treatment for centuries. Distributed throughout eastern and central U.S., southern Canada, its extract has been widely used by many herbalists and physicians as an immune system stimulant. Hence, it can help against system diseases and increase resistance to infection.

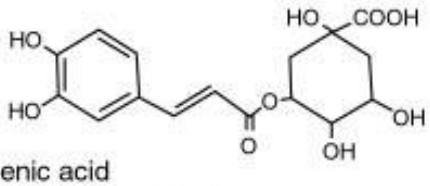
◆ **Photochemistry & constituents**

Phenolic compounds	• phenylpropanoids: echinacoside, cichoric acid, chlorogenic acid, etc. (caffeic acid derivatives) • flavonoids: rutoside
Terpennoid compounds	• essential oil components: borneol, bornylacetate, pentadeca-8-ene-2-one, germacrene D, caryophyllene, palmitic acid, etc.
Lipid compounds	• polyacetylenes: trideca-1-en-3,5,7,9,10-pentayne, pentica-epoxide.
Nitrogenous compounds	• alkylamides • alkaloids: glycine betaine
carbohydrates	• polysaccharides: PS I (4-O-methylglucuronoarabinoxylan), PS II (an acidic arabinorhamnogalactan), xyloglucan, fructose, fructam polymers.
Other constituents	• reducing sugars, phytosterols, ascorbic acid, cyanidin glycosides, etc.

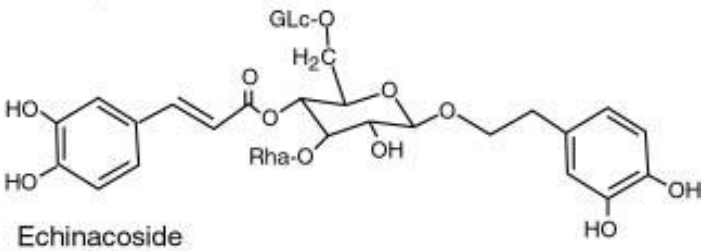
(Bauer and Wagner, 1991)



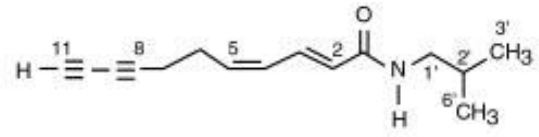
Cichoric acid



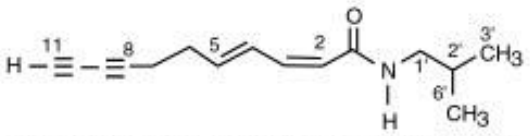
Chlorogenic acid



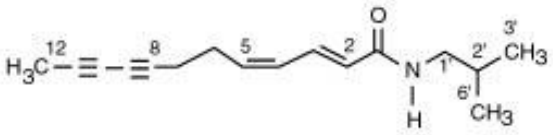
Echinacoside



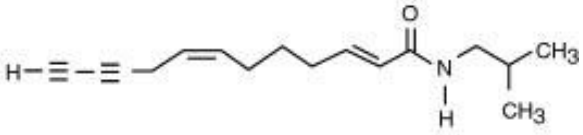
Undeca-2E, 4Z-dien-8, 10-diynoic acid isobutylamide



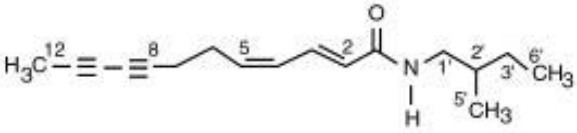
Undeca-2Z, 4E-dien-8, 10-diynoic acid isobutylamide



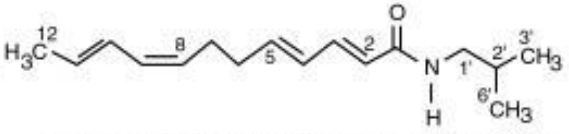
Dodeca-2E, 4Z-dien-8, 10-diynoic acid isobutylamide



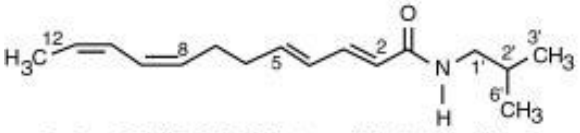
Trideca-2Z, 7Z-dien-10, 12-diynoic acid isobutylamide



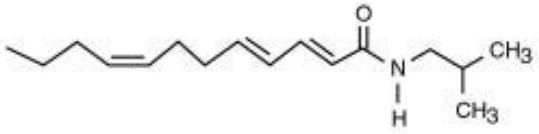
Dodeca-2E, 4Z-dien-8, 10-diynoic acid methylbutylamide



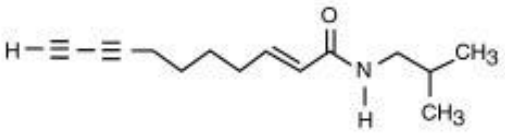
Dodeca-2E, 4E, 8Z, 10E-tetranoic acid isobutylamide



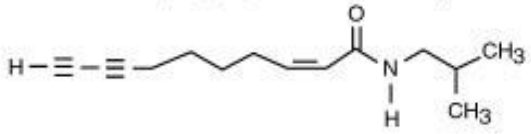
Dodeca-2E, 4E, 8Z, 10Z-tetra acid isobutylamide



Dodeca-2E, 4E, 8Z, trienoic acid isobutylamide



Undeca-2E, ene-8, 10-diynoic acid isobutylamide



Undeca-2E, en-8, 10-diynoic acid isobutylamide

- **Pharmacology**
  - Anti-inflammatory activity

    In vitro tests showed that alkamides extracted from the root of Echinacea Purpurea have the ability to inhibit COX-I and COX-II enzymes, which act in the metabolism of arachidonic acid to pro-inflammatory prostaglandins. (Phetomedicine, 2002) By blocking the production of inflammatory substance, Echinacea Purpurea is believed to use in the treatment of inflammatory disorders.

  - Antioxidant

    Studies indicated that the caffeoyl derivatives from Echinacea Purpurea provide protection against free radical-induced degradation of type III collagen. (Arzneimittelforschung, 1991) The potency of anti-oxidation differs from each other: echinacoside ≒ chicoric acid > cynarine ≒ caffeic acid > chlorogenic acid. E.P. performs a scavenging effect on superoxide anion, hydroxyl radical and C-, N-, S-centered secondary radicals. As a result, the extract of E.P. can be applied in the topical use of the treatment of photodamage of the skin by UV radiation. (which oxidation stress forms free radicals) (Planta Med. 1995)

  - Cytokine-like activity

    A polysaccharide named acidic arabinogalactan from Echinacea Purpurea was found

effective in activity macrophages to secrete tumor necrosis factor (TNF-α), interleukin-1 (IL-1), IL-6, and interferon β (IFN β). (Int J Immunopharmacol, 1991) It also slightly induce the proliferation of T cell. The above actions lead to cytotoxicity against tumor cells and micro organisms. Both in vitro and in vivo tests show acute reaction of activating phagocytes in human.

- Immune system stimulant

  This part of study is somehow unclear.

  Some researches stated that Echinacea Purpurea can enhance cellular immune function such as increasing NK cell's activity, ADCC(antibody-dependent cellular cytotoxicity) of PBMC(peripheral blood mononuclear cells). (Immunopharmacology. 1997) And the activation of macrophages to stimulate IFN-γ production as well cause the activation of T cells. This is the reason why some people consider E.P. a possible treatment against HIV.

  Yet, some other studies showed different results in which E.P. appears to have no effects on T lymphocytes and only a weak stimulation on humoral immunity (B cells).

  No matter it is T cell or B cell that proliferated, overall body immunity is assured to rise under the stimulating effects of Echinacea Purpurea. Among the constituents of E.P., polysaccharides perform an antihyaluronidase action in inhibiting viruses to take over host cells, while the alkamides act as antibacterial and antifungal agent.

- As Infectious diseases medicine

  As long as Echinacea Purpurea has the ability to stimulate immune system, it can help increasing the resistance to viral, bacterial and fungal infections. Certain studies indicated the ethanolic extract of E.P. may contribute to the ability to prevent infections of the upper respiratory tract. Others showed the E.P. herbal remedy is effective in alleviating symptoms in patients during a common cold. (Arzneimittelforschung. 2001) Some animal experiments concluded that pre-treating mice with E.P. polysaccharides appear to provide protection against infections of Lysteria monocytogens and Candida albicans. Excellent protection rate was shown as long as the polysaccharide was administered within short period of infection.

◆ **Safety profile**

- Adverse effects
  - Abdominal upset
  - Nausea
  - Dizziness
  - Allergic reactions: rashes, allergic plant contact dermatitis
  - Ocular adverse effects
  - Cadmium (Cd) toxicity accumulation

    Certain studies of experimental mice stated Echinacea Purpurea decreases

cadmium-induced mitotic activity of liver cells, and increases apoptotic activity of liver cells. Furthermore, the use of E.P. combined with $CdCl_2$ leads to higher concentration of Cd accumulation. Since Cd^{2+} primarily attack kidney and liver, kidney, liver damage and formation of neoplasia should all be concerned. (Virgilijus Zitkevicius, 2010)

- Drug interaction

Some evaluation studies showed possible potential of drug-herb interaction with cytochrome P450 1A2 and CYP450 3A4. (Chem Biol Interact., 2005) Echinacea Purpurea may influence coadministered drugs that are metabolized by CYP450, such as itraconazole, fexofenadine, lovastatin.

Researches showed that taking Echinacea Purpurea may cause hepatotoxicity when used more than 8 weeks. Therefore, hepatoxic drugs, such as anabolic steroids, wafarin, amiodarone, methotrexate, and ketoconazole should be avoided taken with E.P.

- Contraindications

- pregnant women

  Some animal experiments proposed that Echinacea Purpurea may influence fetal development in human because they may interfere with angiogenic activity of the embryo. (De Smet et al., 1993)

- people with allergy

  Related experiments showed that use of Echinacea Purpurea was associated with an increased risk of rash. Patients with asthma or allergy in daisy family should take E.P. with caution.

- patients with autoimmune illness

  Some research suggested that Echinacea Purpurea should be avoided using in patients with progressive systemic diseases, such as AIDS, tuberculosis, diabetes, and multiple sclerosis. E.P. is also not recommended in autoimmune-component illness, e.g. leukemia, lupus erythematosus, collagenosis and other connective tissue diseases. (McGuffin et al., 1997)

- Toxicity

Mutagenicity test: (-)

Carcinogenicity test: (-) (Wagner, 1997; Mengs et al, 1991)

Echinacea Purpurea is reported to be a safe herbal medication with very low toxicity. Acute, subacute, and genotoxicity studies on mice found E.P. to be non-toxic. (Cesk Fam., 1993) In animal experiments, oral doses up to 15g/kg and intravenous doses up to 5g/kg showed no related toxicity. (J Leukoc Biol., 2000) Yet, another mice test did show of LD50 at 2500mg/kg when conducted in injection doses of concentrated E.P. polysaccharide fractions. (J Nat Prod., 2000)