Dynamic Adsorbents

How Can Activated Alumina be Used for Natural Plant Alkaloids?

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Alumina oxide is the sorbent of choice for the separation of basic compounds which include alkaloids, amines, steroids, terpenes, aromatic and aliphatic hydrocarbons. Surprisingly, most separation scientists remain unaware of the benefits provided by alumina and continue to use silica gel for these separations. To that end this paper addresses the role of alumina oxide in the purification of natural plant alkaloids.

There is great structural and biological diversity in the natural plant alkaloids, with more than 100 alkaloids introduced into medical practice. Medicinal and aromatic plants are playing an increasingly important role in the pharmaceutical world in addition to their usage in the cosmetic, fragrance, specialty food and nutraceutical sectors.

There are more than 420,000 distinct plant species, yet less than 10% of them have been fully analyzed. Almost all alkaloids are toxic and most display pharmacologic activity. The isolation and purification of these distinct alkaloid species is a major goal of the biotechnology and pharmaceutical industries with screening procedures for phytochemical analysis beyond the scope of this paper. However, each of the sundry classes of plant alkaloids has been successfully isolated and purified using activated alumina as the sorbent of choice in TLC and flash chromatographic systems. Given that fact that most botanical agents are plant alkaloids TLC plates coated with alumina are the preferred screening tool of choice, as botanicals have species specific fingerprints.

HPLC is an excellent tool for the quantitative analysis of marker compounds in botanical samples. Selecting a desired phytochemical is an appropriate method of establishing a quantitative analysis for a marker compound. The crystallization of alkaloids, both their bases and their salts from different solvents has been phased out as a separation method for isolating and purifying natural plant products.

An alkaloid is a cyclic organic compound in a negative oxidation state found in living organisms. The majority of alkaloids are found in plant species, although there are alkaloids which have also been isolated from animals.
The process of isolating plant alkaloids follows the following sequence of events:

1. Extraction of the raw material from the plant species
2. Separation of the total alkaloids from the other extracted substances
3. Separation of the alkaloids
4. Purification of each of the individual alkaloids

Plant species may contain many unique alkaloids, making the separation process complex. For example the plant species Catharanthus roseus contains more than 90 unique alkaloid substances. The location of these alkaloids within plants varies widely, with the highest concentrations of alkaloid compounds being found in the root system, seeds and bark. Of interest, during the beginning of the vegetation period in the springtime these alkaloid compounds pass from these depot sites into the shoots and then into the plant leaves.

Due to the complex taxonomy of plant species many types of separation techniques have been utilized for isolating and purifying plant alkaloids. Separation may be achieved through a combination of extraction, crystallization, chromatography, molecular distillation and other purification processes.

Extraction is the first step in the process. Examples of extraction solvents currently used to disrupt plant species to yield alkaloids are hexane, methyl acetate, acetone, methanol and hydroflurocarbons such as 1,1,1,2-tetrafluoroethane. Some of these solvents have high boiling points and the elevated temperatures used in the distillation process can degrade some of the desired plant alkaloids.

The goal in using liquid chromatography for the purification of plant alkaloids is clear. Once alkaloids are extracted and ready for purification, they are ready to be eluted. The crude alkaloid extract is mixed with an eluent known as the mobile phase and placed in contact with a solid adsorbent known as the stationary phase to progressively and selectively remove various compounds held on the adsorbent. The particular alkaloid of interest can then be collected in essentially pure form by monitoring and collecting the solvent eluate as it is recovered from the adsorbent. As the solvent flows through the column, it carries the crude material along with it, but the various components of the crude material are carried along at different rates owing to the different affinities that those components have for the adsorbent/solvent pair.

The development of thin layer chromatography began with a desire to isolate unique plant alkaloids. TLC began in 1938 when Izmailov and Shraiber separated plant extracts using aluminum oxide spread on a glass plate.

For the extraction and purification of alkaloids alumina oxide is the sorbent of choice. Alumina possesses both Lewis acid and basic sites and is excellent at adsorbing plant alkaloids, possibly through strained Al-O bonds. The sorbent activity of alumina is modified by altering both the conditions of temperature and hydration. Alumina oxide becomes activated by heating to a specified temperature for a defined time. The optimal activation temperature for alumina is unclear but fully activated alumina for coating of TLC plates can be produced by heating at 150-200 C for a few hours. The activity of alumina can be lowered by adding precise amounts of water.

The activity of alumina may be defined according to the Brockmann scale. Using this scale the addition of 3% water is characterized as Brockmann II, the addition of 6% water is Brockman III and the addition of 10% and 15% water respectively leads to Brockmann IV and Brockman V. Therefore, the lower the amount of water mixed in with the alumina oxide, the lower the Brockman level and the greater the power for alumina to act as a sorbent agent.

Working with plant alkaloids the solid adsorbent is usually a polar material, preferably in particulate form and normally packed in a column to form a bed. The solvent entrains or dissolves the composition to be treated and transports it through the column, specifically through the adsorbent material packing the column. Although the solvent may move passively through the packed column using gravity, most extraction processes of plant alkaloids today use the technique of flash chromatography in which the solvent is driven through the column using a pump or some other means to create a positive (superatmospheric) pressure at the inlet end of the column.

The type of activated alumina used as the adsorbent will be selected based on pore size, particle size and pH. In turn, the decision on which activated alumina to use will be based on the characteristics of the plant alkaloids, such as the compound polarity, solubility, molecular size and shape. Active aluminas are quite sensitive to the differing shapes of various aromatic hydrocarbons and some of their derivatives, permitting an excellent separation of many aromatic isomers. The weight ratio of the composition to be treated to the adsorbent is typically in the range of from 20:1 to 1:2, and is preferably in the range of 1:1 to 4:1.

At this stage unique alkaloids can be collected and made available for further testing regarding biological activity, structure analysis and determination of therapeutic utility.

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