

The apparatus herein shown for this purpose is not quite perfect, but will serve, and can be constructed at small cost.

In talking of all this, my mind goes back forty years or more to an old German druggist friend who called me in to consult with him about the sale of his store. In his laboratory was a pharmaceutical coal-burning stove, which was a miracle of completeness as to the need.

I constantly think of him—this old, long dead friend of mine, as the most modern of all my druggist acquaintances, and this thought is always fruitful of the hope that he may live again and always in his followers.

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### DRUG CLERKS AND BELLADONNA.\*

BY DR. FRED B. KILMER, PH.M.

Something like half a century ago, there was assigned to a young clerk working in a drug store, the task of pounding belladonna in an iron mortar. The root was refractory, the day was hot. The job was not well done, but during its progress the dust from the root smeared his face and reached his eyes. The result was a pair of distended pupils and a dimmed vision.

The lad's mother, in great alarm, visited the druggist, who explained that this was the natural action of belladonna when ingested into the eye, and added the reassurance that it would pass away in a day or two, and it was so.

This lad was the writer, and that experience gave to him a life long interest in the drug.

Before, and since that time many a drug clerk has been brought vividly to a realizing sense of the power of belladonna to dilate the pupil of the eye.

More than one hundred and fifty years ago a drug clerk in the City of Hamburg, Germany, had a similar experience, the final outcome of which forms an important link in the history of the mydriatic action of belladonna.

This is the beginning of his story:

"When a novice in the Hamburg pharmacy of my uncle, Ohrtmann, Dr. Reimar desired some extract of belladonna. The fresh herb, with its flowers and fruit, having been finely comminuted, the better to boil out and extract the tincture, a bit of herb or drop of berry juice unfortunately splattered into my right eye.

"Realizing this, I attempted in vain to remove the foreign irritant from the eye with the finger. Hardly had three minutes of the hour elapsed, the irritant action having ceased meanwhile, when a mistiness arose before the eye, which increased little by little. After quarter of an hour there was present total blindness without any pain, the other eye remaining intact."

The clerk sought the counsel of Dr. Reimar, the prescriber of the drug, and by proper treatment in three weeks his eye "was restored to its pristine integrity."

Reimar informed him that it was known that the ingestion of belladonna would produce mydriasis, but he was surprised to learn that the external application of the drug would produce this result.

The discussion of the matter with Dr. Reimar resulted in the suggestion that

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this peculiar power of belladonna might induce a harmless and temporary paralysis in the operation for cataract.

Daries, the drug clerk, began a systematic study of the known properties of the plant, searching out the literature and instituting a series of experiments upon animals, tending especially to demonstrate the mydriatic action of the drug.

Dr. Reimar has been cited as the discoverer of the mydriatic action of belladonna. Daries believed himself to be the discoverer of this peculiar power.

As a matter of fact, the mydriatic action had been known through the ages, and had been forgotten, or else put aside.

This accident of the Hamburg drug clerk led to the demonstration of the value of belladonna in operations upon the eye, and this should inspire our admiration.

Daries' work forms the basis of a thesis delivered by him as a candidate for the Degree of Doctor, at the University of Leipzig. His thesis bears the following redundant title:

"CONCERNING ATROPA BELLADONNA  
BY THE AUTHORITY OF THE MOST GRACIOUS ORDER OF PHYSICIANS  
UNDER THE DIRECTION OF  
MASTER ANTHONY WILLIAM PLAZ  
PRIMARIUS OF THERAPEUTICS, DEAN OF THE MEDICAL  
FACULTY, SENIOR MEMBER OF THE NATIONAL SAXON  
ACADEMY, MEMBER OF THE BOARD OF GOV-  
ERNORS, "GREATER CHIEF" COLLEAGUE OF  
THE COLLEGE, MEMBER OF THE ACAD-  
EMY OF NATURAL CURIOSITIES.

THE AUTHOR, PETER JOHN ANDREW DARIES, BACHELOR OF MEDICINE,  
OF PARCHIMO-METROPOLITANUS,  
WILL DISPUTE FOR THE DEGREE OF DOCTOR, ON AUGUST 30, 1776."

Leipzig—From the Langenheim Printing Office.

A printed copy of this thesis is in the Library of the Surgeon General at Washington, and to this copy the writer was granted the courtesy of access. The pamphlet comprises forty pages, shows marks of age, and is evidently one of a few printed for use at the time of conferring the degree. One concludes that there are not many copies extant, as it is not generally referred to in the literature of the drug.

By permission of the Surgeon General a photostat copy of the book has been made, and a translation attempted, which it is hoped may find a place in some pharmaceutical library.

The thesis, written in Latin, bears evidence of hasty preparation; at times the language is quite obscure. The references cited are very numerous, but frequently in the citation the name of the author is put down without any indication as to where the citation may be found.

Daries evidently did not search the ancient or classical writers, his citations being mainly those which in his time were modern.

In his introduction Daries states:

"The hodgepodge of books which treat of poisons is so great that the most celebrated Hahn was pleased to call this century the "toxophilic," which is seen to be a most suitable name.

"I have especially read that belladonna is a poison, from the use of which any physician, no matter who, may prudently abstain (Blackwell)."

"Nay, more—for Lewis rejoices that it was abrogated by all authority, and was also rejected in Belgium because of many negative trials (Van der Haar).

"Hahn has said 'the question to be put is whether it is granted to an honest physician to use poisons?'

"But despite this reputation, I cannot see why I may not write of the very active poison and medicine—belladonna. Nothing seems to stand in the way of this, and I may have the good fortune to say something new concerning the effects of the drug."

Daries' own summary gives a clear evidence of his thesis: "I will first give the various names of belladonna, next the botanical characters, then the constituted principles and official preparations, then the salutary and toxic effects will be expounded, and I will adhere chiefly to the powers of the roots, leaves, berries and seeds, with the additions which are discovered after death by autopsy. Then I may add what I, myself, have observed, and last of all will speak concerning the antidotes of belladonna."

Section I of the Thesis is of sufficient interest to reproduce:

#### ONOMATOLOGIA.

"To begin with the name, it will be necessary first that we harmonize about the nomenclature of the plant. That is, about the derivation of the original roots of the given name of this drug. Before everything else we wish to keep by the beauty of language, a subject which is most to be considered.

"*Atropa Belladonna* Linnae is, according to Bauhin, a solanin narcotic poison, the fruit of which resembles that of a black cherry. That the name 'Atropa Belladonna' is Greek, every one will readily understand who is acquainted even to a slight degree with the rudiments of the beautiful Greek language, when hearing the name pronounced, that is, if he does not become disgusted with the Greek letters—*Ētuvxvokevavonesadoyys*.

"The drug is named *Belladonna*—by Tournefort, Clusius, Matthioli, Tragus, Dioscorides, Raii.

"*Atropa*—by Royan.

"*Solanum furiosum*—by Camerar. Letale, by Lobel, Dodon, Clusii, Thalii.

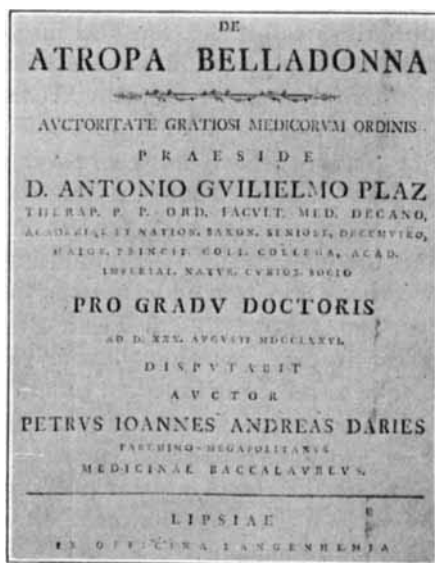
"*Solanum maniacum*—by many writers.

"*Belladonna* I. B., *Solanum bacca nigri*—by Tabern, is a black berry similar to a cherry.

"*Solanum cosmeticum*—by Weinman, Hoffman, Opsago, Gerard.

"Beautiful wife—by Tournefort.

"German names: Waldnachtschatten, Schlafberere, Tollbeere, Irrbeere,



Title Page Reproduction Daries Thesis on Belladonna.

Walkenbaum, Marienkraut, Tollkraut, Tollwurtz, Tollkirschen, Schweintodt, Saukraut, Wuthbeere, Teufelsbeere, Willbeere, Wiedbeere, Windbeere.

"English names: Dwale, deadly raging or sleeping nightshade.

"French names: Morelle marine, Belledame.

"Italian names: Solatro maggiore, Belladonna.

"Belgic names: Groote nachtshaad oft Dulcruyt, Dulle, Besien.

"Spanish names: Yerva mora major.

"Lusitanic names: Ayura, erva, mora.

"Bohemian names: Lilek Wetsy, Psy, Wino.

"Polish names: Pfinki, Moszenky, Pfię Wisnie, Mickonky.

"Hungarian name: Zepzolo.

"Danish names: Natskade, Sovv Boer, Swine urz.

"The belladonna, with its cherry-like berries, possesses such a disagreeable, disgusting odor that beasts avoid it as they would a snake or mad dog. Some authorities call it "cussan" because of the juice of the plant that is made with distilled water, a liquid which Italian women are using to get rid of the wrinkles in their faces, and to beautify themselves; that is, to make pale their dark, rosy cheeks; it is also applied in cases of frigidity."

"Others believe, for this reason, that under the influence of the drug there are produced dreams about beautiful women and virgins.

"But Apuleius insists for certain that this name—"belladonna," was corrupted, and that death and sleep-producing is the name—furious and maniac-making, because it brings on all symptoms with it."

The nomenclature of such a drug plant as belladonna, is of interest by reason of its intricate confusion. Daries' list is the result of an industrious search, and may be taken as an accepted résumé up to his time.

It may be noted that in many instances the names given in ancient literature were also applied to other narcotic solanums. It is likewise notable that in many instances the common, or popular, name is expressive of the peculiar power and action of the drug. The name often gives a hint of the legends and lore which surround belladonna.

Daries' description of the plant is made from direct observation of a living specimen. With a slight change of phraseology it would be accepted in our day. He speaks of a plant of goodly proportion, three ells in height.

In Section III, "Principia Constitutiva," the views of many authors as to the physiological action of the drug are given.

The curtain is raised on the mystic beliefs of the time, in an attempt to account for the, to him, unexplainable action of belladonna.

"Vegetable poisons act chiefly by a meandering vaporosity."

"The principle at once hot and sharp afflicts the nerves by tearing, and agitates the blood, lymph and other humors and spirits."

"Stenzel accuses the fault of virulence to inhere in the sulphur which, grave-olent and vaporous, infects and contaminates the fluids of the brain and parts of the nerves, suppresses their powers and stops vital motion."

Belladonna had been placed under the ban by the medical men, because of its highly poisonous power. Daries therefore puts forth a strong effort in the section

"The Salutory Effects of Belladonna," to defend his thesis. It is the longest section and is overflowing with citations.

Observations upon the use of belladonna in cancer are the most numerous. The use of belladonna in cancerous affections goes back to ancient times and continues down to our day.

The use of belladonna as a soporific or anesthetic prior to surgical operations, is noted.

"The juice of belladonna berries is used for preparing a color."

The plant is used "against the diseases of cattle, especially the pestilence." It is "a preservation for animals."

"Deer are delighted with the leaves."

In a later section Daries seems to show a poisonous action against cattle.

"The poisonous power of belladonna lies in the entire plant, more, however, in the berries and roots than in the leaves."

The dog, the rabbit and the cat are not poisoned by the ingestion of belladonna into the stomach.

Daries attributed differing powers to the root, the leaves, the berries and the seeds, and devotes a section to each of these parts of the plant. Each part is poisonous in a varying degree, each part has a somewhat different physiological and therapeutic action.

The action and properties of the flowers were unknown to Daries. This in a sense is true to-day. The action of all parts of belladonna has been thoroughly studied save that of the flowers. I have never noted any reference to the presence or absence of alkaloids in the flowers of belladonna.

In recent times a sensational article appeared in public print tending to spread an alarm as to poisonous honey gathered by bees from belladonna and other solanums. This was an exaggerated alarm. If there is any alkaloid in the flowers of belladonna, the bees are immune to its action. Great quantities of honey gathered from the poisonous solanums have been eaten without untoward results. In a cultivation of belladonna, covering a large acreage, bees from a nearby apiary continuously visited the flowers, and the stored honey was eaten without harm.

It might be an interesting study for some drug clerk, following Daries, to make a special investigation of the constituents of belladonna flowers.

In Daries' thesis, and in all the literature of belladonna, whether ancient or modern, the poisonous action of the berries is the most numerous.

Certain authors ascribe poisonous power only to the berries. The luscious looking berries, tempting to the eye and the taste, fill the annals of belladonna poisoning.

The crowning work of Daries is quaintly told in the section of his thesis entitled "On Experiments Undertaken."

"Some one may now take me to task as to whether I am troubled concerning the remedy which must be devised, that may produce the desired effect better in a given disease. These various symptoms concerning which I have copiously labored, led me to think likewise of experiments conducted on animals, to see whether that phenomenon observed in my eye might also be caused similarly in animals. Therefore, about to explore the powers of belladonna myself, I sprinkled into the right

eye of a domestic cat the juice expressed from the herb, and in the left eye the juice of the berries. But it escaped me."

"If a cat or owl is placed in an utterly dark place, no light of any kind, and no light to appear, it is nevertheless reflected from the eyes, as soon as ever so little light is admitted.

"The eyes of these animals, before others, have the singular property that not only is the pupil much wider than the freer iris, and nowhere coherent to the cornea, but even the finest are pleased and moreover carry more also of aqueous humor between the cornea and crystalline humor, more remote from the pupil, but nearer to the retina, while endowed with non-pigmented choroid, and an obscure but pale flavescent or cerulean one. The conjunctival tunic of this cat, moistened with these juices by means of a feather, one hour having hardly elapsed, the uvea became dilated, much more the right than the left, so that the chink was more than tenfold larger, and indeed assumed a circular shape, when formerly this had been oblong. In the eyes, moreover, nothing was seen of disease or cloudiness. Left to itself, the cat staggered as if drunk from the beginning, but a little later it walked with its accustomed gait, its head hanging, and tried with its fore feet to remove the application from its eyes.

"After an interval of two hours the phenomenon wholly disappeared, and the narrow longitudinal chink was restored to both eyes.

"With this experiment repeated with the dry herb in the right eye and the juice of the berry in the left, in a little while the uvea was dilated to the former circle. On the following morning the dilation of the pupil had again vanished. Therefore, instituting this experiment for the third time, the same result was obtained, but with this difference, that twelve hours having elapsed the pupils remained immobile.

"From this fact the cat was subjected to the anatomist's knife of my impartial friends, the distinguished Hebenstreit and Gerischer.

"In the alimentary canal, in the chest, abdomen and brain, no alterations were found. But on investigating the eye, the uvea, quite towards the wall of the sclerotic, to which the choroid adheres, was flaccid and at the same time retracted in such manner that the pupil was tenfold larger than is found in the normal cat. The aqueous humor was clear, the vitreous indeed thin, almost watery, but nevertheless was quite soft."

"Likewise Rossi writes, 'dogs, cocks, chickens and small birds are disturbed by no sign of inflammation nor by pain, when their eyes were touched with a feather wet with the juice.' With two of the birds, a swallow and a lark, this experiment was carried out in the prescribed manner, and it is testified that this agrees perfectly with the truth, for the two birds developed no symptoms, the juice applied being gradually absorbed by the lacrymal points."

"This phenomenon observed in the eyes of the cat, does it fully correspond to the observation of Raius, which I have given elsewhere?"

"The illustrious Van Swieten contends that paralysis of the pupil following a specimen of the *Solanum furiosum*, applied to an ulcer, was readily able to relieve it."

"This opinion, compared with the judgment of Dr. Reimar, concerning the application of belladonna as bound to induce a harmless temporary paralysis of

the eye in order that extraction of the lens may be more readily carried out, seems to me to agree excellently. Finished, therefore, is the copious discussion concerning the powers of belladonna, the salutary as well as the poisonous, which although possibly too lightly composed for a polished disputation, I submit to the judgment of the World of Letters."

Another drug clerk, more than forty years after Daries, in preparing a prescription, had a similar accident that led to important results in the study of the mydriatic action of belladonna and allied solanums. This is the story of Runge, afterwards famous for his work on aniline colors:

"In 1810 I, a pastor's son, from the country near Hamburg, was sent to Lubeck, and placed in the Rathsapotheke as an apprentice.

"It was during this service that I had to prepare a medicine according to a doctor's prescription, in which a decoction of the juice of hyoscyamus was to be dissolved in water. Preparing the medicine in a mortar, a drop accidentally got into my eye. I experienced no pain, and did not observe any alteration until sensations of light flashes caused me to go to the looking-glass. How great was my astonishment when I saw the change that had taken place in my eye. The iris had almost wholly disappeared, and the eye looked precisely like that of a man suffering from amaurosis. The power of vision was also greatly weakened, as I noticed when I closed the unaffected eye. I don't know why this state of things did not raise any fears in me. After lasting a few days, the abnormal condition disappeared, the power of vision returned, and also the normal proportions of the iris, so that both pupils appeared again of equal size."

This drug clerk, knowing nothing about the work of Daries, now began an investigation as to the cause of his experience. The first use he made of his discovery was to dose a fellow townman's eyes so that he could escape military duty by reason of defective vision.

He tells his story as follows:

"At the University in Jena, I became acquainted with Dobereiner, and discussed with him my researches about vegetable poisons, especially the *solanaceae*. Dobereiner appeared pleased with the methods instituted by me, and the results of my investigations; he constantly stimulated me to new researches.

"About this time I met Goethe, at the instigation of Dobereiner, who had told the poet that by experiments upon cats I had found a method of ascertaining with certainty whether or not a poisoning with stramonium had occurred. Goethe had thereupon expressed the desire to meet the young chemist, and to see the demonstration of his discovery.

"When I crossed the market square in the afternoon, dressed with a borrowed frock coat and stovepipe hat, and carrying the cat under my arm, I created a universal sensation. The boys who were loitering about the place, at the cry 'Doctor Poison,' suddenly came towards me, and surrounded me. To those joking at my fantastic appearance I said, 'Let me in peace. I am attending to some important business. I am going to Goethe.' I was instantly released.

"Coming to Goethe's house, I was led into the reception room, and soon seated before the poet. His lofty, handsome and powerful presence made such an overwhelming impression upon me, that, all in a tremble, I handed him the cat, as if

I wanted to defend myself. 'Ah! so,' said Goethe, 'that's what is going to be the future terror of the poison-mixers. Just let me look.'

"I then turned the cat's head so that the light struck both eyes simultaneously, and the difference between the eyes could be readily seen. Goethe was greatly surprised. Alongside of the small slit in one eye, the round great opening in the other presented a very striking difference. In consequence of a somewhat large dose, the entire iris had almost become invisible, thus enhancing this singular aspect.

"'How did you obtain this effect?' asked Goethe. 'With hyoscyamus, your excellency,' I answered. 'I have placed the unmixed juice of the pounded herb in the eye, therefore the action is so strong.' 'Dobereiner told me,' said Goethe, 'that hyoscyamus, belladonna and stramonium act alike, and that you have ascertained that the active toxic principle is contained in the plants in all of their parts, from the root to the blossom, fruit and seed, How is it with other plants, especially those of an affiliated relation?'

"A friend of mine, Dr. Carl Heise, induced by the peculiar action of the stated plants, has shown in an elaborate work that only the plants of the three orders mentioned above affect the pupils in a mydriatic manner. He has tried the action of innumerable other plants on the eye, and found them all to be inert save a few which produced the reverse of mydriasis, *viz*: a contraction of the pupil, such as *aconitum*.

"'Well,' Goethe said, 'there is a chance to discover the proper antidote for the toxic action of belladonna. Try this, and apply both antagonistic plants either simultaneously or one after another to the eyes of a cat. Observe the result. The matter is not without difficulties, but you will overcome them.' "

Runge tried to utilize his discovery practically at once, for he recommended in his inaugural dissertation ("De Novo Methodo Veneficium Di judicandi," Jena, 1819), in a case of suspected solanum intoxication, to place a drop of the urine of the poisoned person into the eye of a cat. The word "atropine" does not seem to have been known to Runge, for the solanacea alkaloidal bodies, isolated approximately by him, he called "koromegyn" (Greek-magnifier of pupil). The alkaloid atropine was isolated properly in 1830, by the apothecary Mein, and independently of him in 1832, by Geiger and Hesse, while Liebig determined its chemical formula.

Here we have a series of ordinary drug clerks, without the advantages of modern education or modern laboratories, with no knowledge of modern pharmacological methods, carrying forward a most important drug research that in its final outcome bestowed unmeasurable blessings on the human race.

The end was to establish the mydriatic action of belladonna and the mydriatic solanums for all time, and to give to the world—Atropine.

There are many worlds yet to conquer, even in belladonna. On my desk as I write is a jar of sticky stuff that was extracted from belladonna without the use of alcohol or other ordinary extractive solvent. It is a gluey mess. Its mydriatic action is more than one hundred times that of an equal weight of the drug. What is it? What is its use? I do not know.

There are many drugs on our shelves of which we know but little regarding their constituents, properties, or uses. They await some drug clerk, accompanied by the drug-store cat, to enter in and occupy the land.