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PHARMACEUTICAL DRUG DISPOSAL SYSTEM

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1	2020-11-19	N. Miller	N. Miller	

Executive Summary

GiGi Supplies approached HRL Technology Group to assist in devising and testing a Pharmaceutical Drug Disposal System, based upon Activated Carbon as adsorbent.

This report outlines the literature study, tests, and analyses, and proves the favourable outcome of the tests. It is very evident from the literature study that a wide range of pharmaceutical drugs can be adsorbed onto Activated Carbon. Activated Carbon is commonly used in medical fields to adsorb various chemicals.

Activated Carbon has been proven to adsorb large amounts of pharmaceuticals from aqueous media (e.g., simulated gastric juice) by small amounts of Activated Carbon in a matter of minutes.

Pharmaceutical drugs that have been adsorbed onto Activated Carbon are not easily removed by solvents like water or ethanol. The pharmaceutical drugs are rendered unavailable and unusable for all practical purposes – refer to Title 21 Code of Federal Regulations, Part 1300, below.

§1300.05 Definitions relating to the disposal of controlled substances.

Non-retrievable means, for the purpose of destruction, the condition or state to which a controlled substance shall be rendered following a process that permanently alters that controlled substance's physical or chemical condition or state through irreversible means and thereby renders the controlled substance ***unavailable and unusable for all practical purposes****. The process to achieve a non-retrievable condition or state may be unique to a substance's chemical or physical properties. A controlled substance is considered "non-retrievable" when it cannot be transformed to a physical or chemical condition or state as a controlled substance or controlled substance analogue. The purpose of destruction is to render the controlled substance(s) to a non-retrievable state and thus prevent diversion of any such substance to illicit purposes.*

The use of Activated Carbon seems to be a natural choice in the use of Pharmaceutical Drug Disposal systems.

The literature study performed on the various aspect of the Pharmaceutical Drug Disposal System showed that Activated Carbon is well-known for its capability to adsorb various chemicals, and specifically pharmaceutical drugs.

The specific component was identified as important and tested in this study: Activated Carbon.

Several tests were performed to determine the suitability of the activated carbon: Iodine Number (to assess the active surface area), the Particle Size Distribution, a Dissolution Test with Model Pharmaceutical Drug: Oxycodone HCl, and finally a Time-Dependant Adsorption Test with Model Pharmaceutical Drug: Oxycodone HCl.

The adsorption rate is fast (as little as 20 minutes under certain circumstances) and complete (at least 99.99 % effective).

Table of Contents

1 Introduction

GiGI Supplies contracted HRL Technology Group to assist in the development and evaluation of an environmentally friendly pharmaceutical drug disposal system.

The pharmaceutical drug disposal system is based on the principle that activated carbon adsorb a large variety of chemicals on its surface – and Activated Carbon usually have a huge surface area, most often larger than 1000 square meters per gram.

There are several specific reasons to create a successful pharmaceutical drug disposal system:

1. Reduce the environmental and biological impact of pharmaceutical drugs
2. Reduce the illicit use of pharmaceutical drugs
3. Reduce the availability of illicit pharmaceutical drugs
4. Reduce the inadvertent intake of pharmaceutical drugs by children, mentally handicapped persons, or other people with other frailties or disabilities
5. Safe disposal at various facilities, including pharmacies (drug stores), aged care facilities, care facilities for frail or handicapped persons, police stations, hospitals, clinics, and various other facilities where pharmaceutical drugs need disposal

This report examined a combination of Activated Carbon and additives to safely dissolve, deactivate, and adsorb pharmaceutical drugs.

Please note that in some literature the terms 'Activated Charcoal,' 'Activated Carbon,' and 'Active Carbon' are used interchangeably.

HRL Technology Group is an accredited facility; HRL Technology Group holds accreditation for ISO 17020, ISO 17025, and ISO 9001:2015 (NATA Accreditation Number 561 and BSI Accreditation Number FS65166). The literature study, analyses, and tests were performed using Good Laboratory Practices.

2 Overview

This study focused on several areas:

1. Literature Review
2. The surface area of the supplied Activated Carbon
3. The ability to dissolve, deactivate, and adsorb a model pharmaceutical drug
4. The time required to adsorb a model pharmaceutical drug
5. Background information about the Activated Carbon

3 Literature Review

The literature overview focused on the traditional use of Activated Carbon, and how it supports the use of Activated Carbon as an adsorbent of pharmaceutical drugs, as well as other, similar compounds.

3.1 Book: Activated Carbon by Harry Marsh & Francisco Rodríguez Reinoso

ISBN: 9780080455969, 0080455964
Page count: 554
Published: 12 July 2006
Format: E-book
Publisher: Elsevier Science
Language: English
Author: Harry Marsh, Francisco Rodríguez Reinoso
Editor: Francisco Rodríguez Reinoso

This book refers Activated Carbon as being 'as old as history itself and would be known to Hippocrates, the father of medicine. the most early of recorded applications include their use as a medicine to relieve digestion problems which continue today in the removal of overdoses of drugs from stomachs.'

This book also indicates that the 'most dramatic application of charcoal was in World War I with its use in gas masks for the protection of soldiers against chlorine, phosgene, and mustard gas in trench warfare… It was reported at that time that these respirators were more effective against chlorine (Cl2) and phosgene (COCL2) than with mustard gas (1,1-thiobis(2-chloroethane))… because of its size and shape, would be adsorbed more slowly than the smaller molecules of chlorine and phosgene.'

The authors describe some tests that are generally used to determine the suitablility of Activated Carbon for its intended use. Test methods have been developed and approved by various organisations and the methods are freely available. These organisations include:

- American Society for Testing Materials (ASTM)
- The American Water Works Association (AWWA)
- The International Organization for Standardization (ISO)
- The Deutches Institut für Normung (DIN)

Some of the tests include:

- Physical Characterisation
    - Bulk Density
    - Real Density
    - Apparent Density
    - Particle Size Distribution
    - Mechanical Strength
- Chemical Characterisation
    - Moisture Content
    - Ash Content

  - Ignition Temperature (kindling point)
  - Self-Ignition Test
  - pH Value
  - Water-Soluble Content
- Adsorption Characterisation
  - Carbon Tetrachloride Activity
  - Benzene Adsorption
  - Iodine Adsorption
  - Methylene Blue Adsorption
  - Phenol Adsorption
  - Molasses Decolourisation
  - Butane Adsorption
  - Phenazone Adsorption
  - Specific Surface Area (BET Test, i.e., Brunauer–Emmett–Teller theory)

3.2 Book: Activated Carbon Adsorption by Roop Chand Bansal & Meenakshi Goyal

ISBN: 9781420028812, 1420028812
Page count: 520
Published: 24 May 2005
Format: E-book
Publisher: Taylor & Francis
Language: English
Author: Roop Chand Bansal, Meenakshi Goyal

The authors of this book list some of the following areas as typical liquid-phase applications:

- Food processing
- Preparation of Alcoholic Beverages
- Decolourising of Oils and Fats
- Sugar Industry
- Pharmaceutical Industry
- Recovery of Gold
- Purification of Electrolytic Baths
- Purification of Liquid Fuels

Some more specific applications are listed in Chapter 7 of the book, under the heading of 'Activated Carbon Adsorption and Environment: Adsorptive Removal of Organics from Water'

- Activated Carbon Adsorption of Halogenated Organic Compounds
- Activated Carbon Adsorption of Natural Organic Matter (NOM)
- Activated Carbon Adsorption of Phenolic Compounds
- Adsorption of Nitro and Amino Compounds
- Adsorption of Pesticides

- Adsorption of Dyes
- Activated Carbon Adsorption of Drugs and Toxins
- Adsorption of Miscellaneous Organic Compounds

Once again, the authors mention that 'The activated carbon adsorption of synthetic drugs have been studied with a view to remove them from the human body when taken in excess…'

3.3 Book: Activated Carbon Surfaces in Environmental Remediation by Teresa J. Bandosz

ISBN: 9780080455952, 0080455956
Page count: 588
Published: 27 February 2006
Format: E-book
Publisher: Elsevier Science
Language: English
Author: Teresa J. Bandosz
Editor: Teresa J. Bandosz

The author discusses the use of Activated Carbons as Medical Adsorbents in more detail than the previous authors and mentions that 'Activated Carbons have been used in medicine since ancient times.' The author refers to another book (described in paragraph 3.4 in this report), 'Activated Charcoal in Medical Applications' by David O. Cooney which details activated charcoal's great effectiveness in treating drug overdoses and poisonings in both humans and animals, as well as activated charcoal's ability to reduce the systemic absorption of a vast array of drugs, chemicals, and biochemical substances-including analgesics, antipyretics, sedatives, alkaloids, snake venoms, and bacterial and fungal toxins.

The authors list a table (page 536, Table 1) titled 'Toxic Organic Substances and Drugs Adsorbed by Activated Carbon' and list some of the following types of poisons which can be adsorbed (specifically in humans, but also in animals): strychnine, aspirin, acetaminophen, propoxyphene, phenobarbital, barbital, zolpidem, carbamazepine, mefenamic acid, piroxicam, phenylbutazone, indomethacin, imipramine, desipramine, nortriptyline, doxepin, furosemide, and many more.

3.4 Book: Activated Charcoal in Medical Applications by David O. Cooney

ISBN: 9780367401917, 0367401916
Page count: 608
Published: 23 September 2019
Format: Paperback
Publisher's Press LLC
Language: English

Author: David O. Cooney

The publisher of this book describes it as highlighting activated charcoal's great effectiveness in treating drug overdoses and poisonings in both humans and animals, and this comprehensive, single-source reference brings together vital information from every significant study on the use of activated charcoal for medical purposes – describing all available charcoal products and their characteristics.

The book details activated charcoal's ability to reduce the systemic absorption of a vast array of drugs, chemicals, and biochemical substances – including analgesics, antipyretics, sedatives, alkaloids, snake venoms, and bacterial and fungal toxins.

3.5 Book: Activated Charcoal Antidote, Remedy and Health Aid by David O. Cooney

ISBN: 9781479603367, 1479603368
Page count: 102
Published: 6 October 2016
Publisher: TEACH Services, Inc.
Language: English
Author: David O. Cooney

In this book the author gives an overview of the medical applications of Activated Carbon. The author lists proven applications of Activated Carbon in Chapter 5 under the heading 'Effects of Activated Charcoal on Various Types of Drugs and Poisons.' The list includes the following, and some other chemicals:

- Common Household Chemicals
- Alkaloids
- Aspirin and Other Salicylates
- Acetaminophen
- Hypnotics and Sedatives
- Tricyclic Antidepressants
- Cardiac Glycosides

The author describes more details regarding research done on hypnotics and sedatives, specifically works done by Anderson in 1948, Picchioni's research group in 1966, and later works done by Picchioni, Chin, and Laird in 1974. Other works are listed. The research works indicate, in general, that 'It is clear that the charcoal, …, was effective in lowering blood drug levels.'

3.6 Scientific Publication: Management of Acute Poisoning with Activated Charcoal by Donald G. Corby & Walter J. Decker

Publication: Pediatrics
Authors: Donald G. Corby & Walter J. Decker
Date: September 1974
Volume: 54 (3)
Pages: 324-329

In this publication the authors found that 100 % adsorption of 10 capsules and 85 % adsorption of 20 capsules (each capsule = 32 mg propoxyphene) after only 20 minutes in a 150 mL solution of simulated gastric juice to which 5 grammes of activated charcoal had been added.

3.7 Scientific Publication: Activated Carbon-Based System for the Disposal of Psychoactive Medications by Song et al

Publication: Pharmaceutics
Authors: Song Y, Manian M, Fowler W, Korey A, Kumar Banga A
Date Published: 07 November 2016
Volume: 2016; 8(4):31
doi: 10.3390/pharmaceutics8040031

(This Scientific Paper is Published by MDPI AG, St. Alban-Anlage 66, CH-4052 Basel, Switzerland)

The authors mention that 'Activated carbon is obtained by thermal decomposition of carbon-based materials such as coal, coconut, or wood. The purpose of this activation procedure is to achieve a high internal surface area which is good for the adsorption of the drug from the formulation to the activated carbon. This large surface area is due to the presence of small, low volume pores on the charcoal where the pore size distribution contributes to the efficiency of the activated carbon in the drug adsorption. Activated carbon has numerous micropores in comparison to charcoal which provides maximum bonding surface area for drug binding. This granular activated carbon is already being used in water treatment processes for removal of micropollutants including pharmaceuticals and endocrine disruptors.'

The authors concluded their study saying that 'The effectiveness of the activated carbon-based drug disposal system was examined using three model psychoactive medications. The deactivation system successfully adsorbed and deactivated about 70 % of the psychoactive medications by 8 h and more than 99 % within 28 days and did not release adsorbed drug substances when exposed to large volumes of water or 30 % ethanol. Thus, this unique system is simple, safe, and user-friendly for patients who can deactivate unused or expired psychoactive medications from the comfort of their homes.'

The authors proved that the drugs are irreversibly adsorbed onto the Activated Carbon and cannot be removed by means generally available to the general public.

3.8 Summary of Literature Review

It is very evident from the literature study that a wide range of pharmaceutical drugs, and many other organic and inorganic chemicals, can be adsorbed onto Activated Carbon. Activated Carbon is commonly used in medical fields to adsorb various chemicals to reduce the toxicity (e.g., after an overdose).

Activated Carbon has been proven to adsorb large amounts of pharmaceuticals from aqueous media (e.g., simulated gastric juice) by small amounts of Activated Carbon in a matter of minutes.

Pharmaceutical drugs that have been adsorbed onto Activated Carbon is not easily removed by solvents like water or ethanol.

The use of Activated Carbon seems to be a natural choice in the use of Pharmaceutical Drug Disposal systems.

4 Materials used in this Study

Activated Carbon and several additives were used in this study.

5 Analysis Methods and Results

5.1 Iodine Number

The iodine number was determined using the standard ASTM method: ASTM D4607-14, Standard Test Method for Determination of Iodine Number of Activated Carbon, ASTM International, West Conshohocken, PA, 2014, www.astm.org.

The iodine number is a relative indicator of porosity in an activated carbon. Iodine number may be used as an approximation of surface area for some types of activated carbons.

In this test method a sample of Activated Carbon is prepared; a given excess amount of dissolved iodine (I_2) added to a measured amount of Activated Carbon and after a given period, the excess amount of iodine that has not been adsorbed, is titrated with standardised sodium thiosulphate. The iodine number is calculated from the titration values.

The Iodine Number determination was performed in triplicate and the following results were obtained:

Average	1239	$mg.g^{-1}$
Number of Replicates	3	
Standard Deviation	50	$mg.g^{-1}$
95 % Confidence Interval with a Coverage Factor of 2 (k = 2)	112	$mg.g^{-1}$

5.2 Particle Size Distribution

The Particle Size Distribution was determined using the standard ASTM method: ASTM D2862-16, Standard Test Method for Particle Size Distribution of Granular Activated Carbon, ASTM International, West Conshohocken, PA, 2016, www.astm.org (however, more sieves were used than specified to obtain better distribution curves).

It is necessary to know the distribution of particle sizes of granular activated carbon in order to provide proper contact of gases or liquid in a packed bed of the material. Changes in particle size distribution can affect the pressure drop across the bed and the rate of adsorption in a bed of a given size.

If the Activated Carbon contains a large proportion of small particles it can lead to excessive dust production – this in turn can simply be a nuisance but can also lead to a combustible or explosive atmosphere.

US Mesh Size	Metric Size / (µm)	Percentage Cumulative Retained
5	4000	100.0 %
10	2000	100.0 %
14	1400	71.5 %
16	1180	52.4 %
18	1000	35.2 %
20	850	19.0 %
30	600	3.1 %
35	500	1.5 %
50	300	0.4 %
Pan	< 300	0.2 %

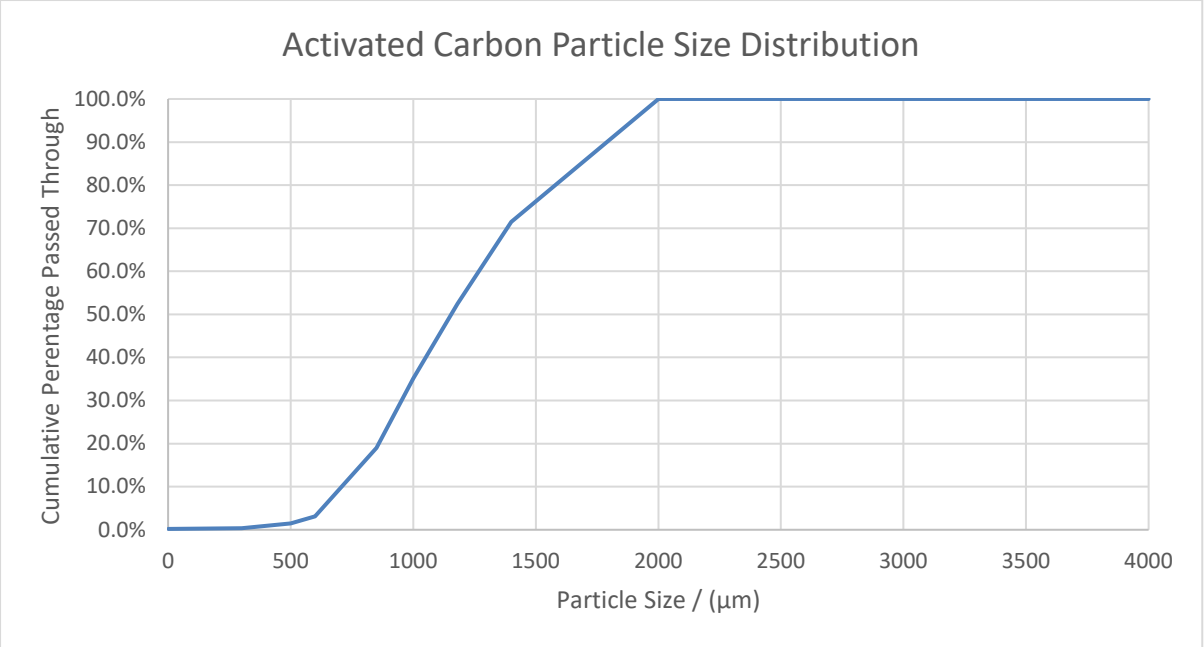

Figure 1: Activated Carbon Particle Size Distribution

The particles are not too small (i.e., there is less than 5 % < 30 mesh / 600 µm).

5.3 Dissolution Test with Model Pharmaceutical Drug: Oxycodone HCl

The test was devised to show the fast and complete dissolution of pharmaceutical drugs with the chosen solvent (Water) and other additives.

Five tablets containing 5 mg Oxycodone HCl each was placed upon a bed containing 5.00 grammes Activated Carbon and 51 mL solvent (water with additives); photos were taken for a period of more than 18 hours.

Three photos are shown in Figures 8 to 10, below, showing the start, after 1 hour (without any agitation), and finally after 18 hours with only minor agitation.

A time-laps video is available on YouTube; the video is private and can only be accessed through the following link: https://www.youtube.com/watch?v=4D7EiDTewSU

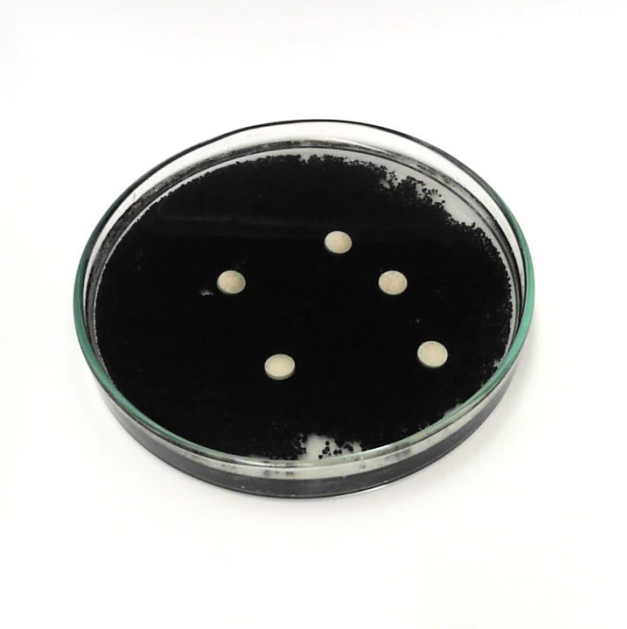

Figure 2: 5 Oxycodone Tablets Loaded onto Activated Carbon Bed - Time 0:00

Figure 3: Oxycodone Tablets Loaded onto Activated Carbon Bed - Time 1:00

Figure 4:Oxycodone Tablets Loaded onto Activated Carbon Bed - Time 18:00

5.4 Time-Dependant Adsorption Test with Model Pharmaceutical Drug: Oxycodone HCl

The test was devised to show the fast and complete adsorption of pharmaceutical drugs onto the activated carbon.

The following solution was prepared and loaded onto 10.01 grammes activated carbon: 20 Tablets, each containing 5 mg Oxycodone HCl, in 200 mL water. The total amount of Oxycodone HCl was 100 mg in 200 mL water, resulting in a concentration of 500 µg Oxycodone HCl per millilitre.

(Note: a large volume of water was selected to ensure the small portions sampled after initial loading would not impact on the outcome. Lower volumes of water can be used in production system with negligible impact to results.)

Two millilitre portions of samples were taken at specific intervals after it was loaded onto the Activated Carbon: 1, 2, 4, 6, 24, 48, 96, and 145.5 hours after initial loading. The amount of Oxycodone HCl left in each two-millilitre portion was determined using High-Performance Liquid Chromatography (HPLC).

HPLC is a technique in analytical chemistry used to separate, identify, and quantify each component in a mixture. It relies on pumps to pass a pressurised liquid solvent containing the sample mixture through a column filled with a solid adsorbent material. Each component in the sample interacts slightly differently with the adsorbent material, causing different flow rates for the different components and leading to the separation in time of the components as they flow out of the column. The various components are detected using specific detectors, tailored to detect the type of compound being investigated.

HPLC Analysis Method

All samples including the reference solution were thoroughly shaken and subsequently centrifuged (3600 rpm for 10 min). The supernatant from the reference standard solution was suitably diluted (with water) to prepare a set of calibration standards (0.50 – 50.0 $\mu g.ml^{-1}$). Samples (5.0 µL) were injected as received and analysed using the basic method as supplied. A Reverse-Phase column (Phenomenex® Synergi RP Fusion 250 x 4.6, 4.0 µm) was used to separate the active ingredient.

Calibration

Figure 11, below, shows the calibration graph for the determination of Oxycodone HCl.

Sequence Summary Report (Short) Agilent Technologies

Calibration Update: 2020-11-06 08:18:49+02:00

Compound: Oxycodone
Signal: DAD1A
Exp. RT: 12.692
Corr. Coeff.: 0.999961
Residual: 1.90091
RF RSD%:
R^2: 0.99992
Formula: y = ax + b
a: 10.88556
b: 1.16663
c: 0.00000
d:

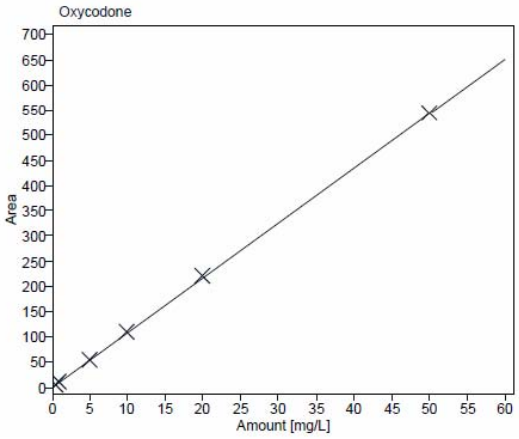

Figure 5: HPLC Calibration Graph for Oxycodone HCl

The table shows the Time after Loading, the Oxycodone HCl concentration left in solution, and the percentage adsorbed.

Time after Loading (Hours)	Oxycodone HCl Left in Solution / (µg/mL)	Percentage Adsorbed
1.0	9.9143	98.02 %
2.0	0.4291	99.91 %
4.0	0.0885	99.98 %
24.0	0.0601	99.99 %
48.0	< 0.05	> 99.99 %
72.0	< 0.05	> 99.99 %
145.5	< 0.05	> 99.99 %

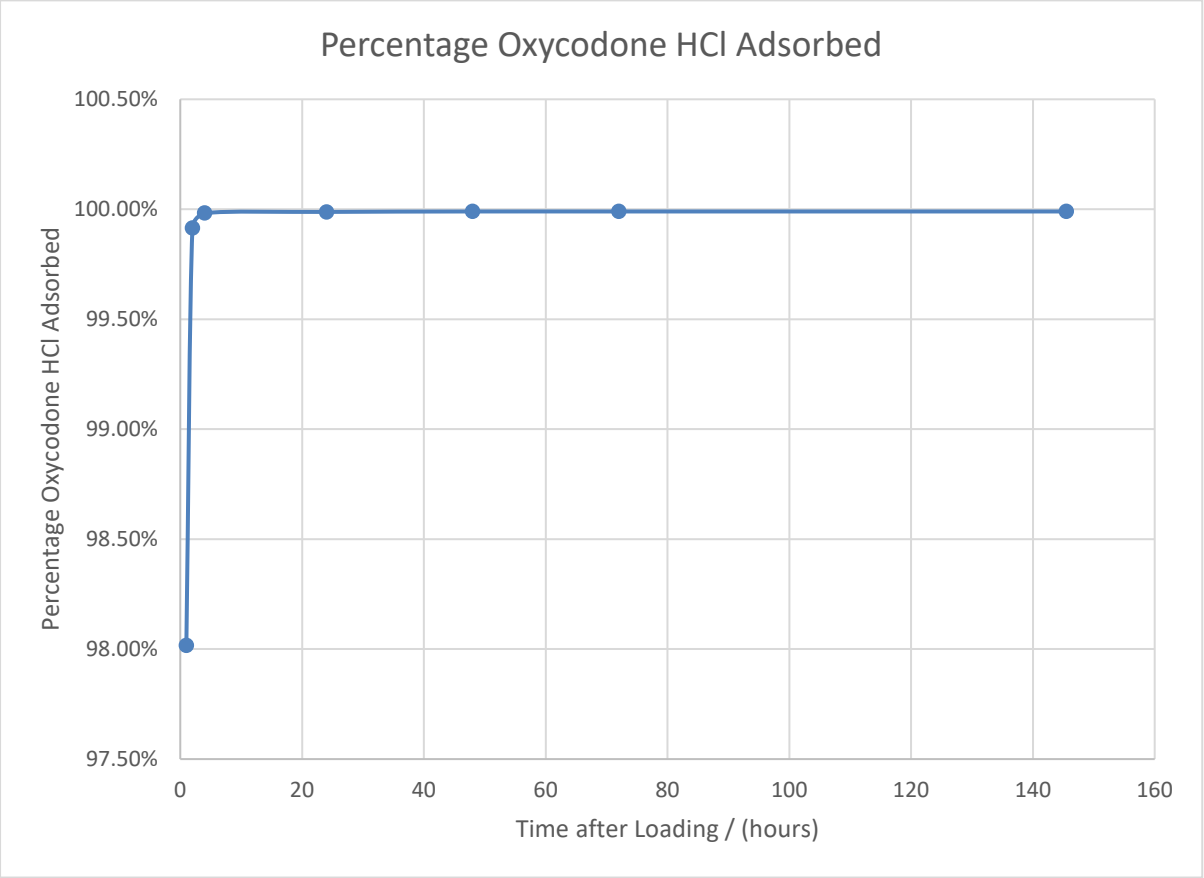

Figure 6: Graph Showing Fast and Complete Adsorption of Oxycodone HCl on Activated Carbon

Results

The Time-Dependant Adsorption Test showed that Oxycodone HCl adsorbs very quickly (more than 98 % in one hour) and completely (more than 99.99 %) onto the activated carbon.

Other studies have found similar outcomes (see paragraph 3.6) where up to 100 % of the active ingredient was adsorbed in only 20 minutes, depending upon the loading.

The study concludes that 10 grammes of Activated Carbon can easily adsorb more than 20 tablets successfully within 24 hours.

The capacity of the activated can be extrapolated, i.e., 500 g Activated Carbon will be able to adsorb more than 1,000 tablets, while 1 kg of Activated Carbon will be able to adsorb more than 2,000 tablets.

5.5 Dissolution Test and Time-Dependant Adsorption Test

The Dissolution Test showed that the (photos in Figures 8 to 10, above), showed that the tablets were disintegrated after only 18 hours with only minor agitation. The Time-Dependant Test showed that the 98 % of the active ingredient was adsorbed within one hour. The photo, Figure 9, showed some material left after one hour – this should be only some of the excipient material left. A little agitation would break up the excipient material completely and ensure complete adsorption of the pharmaceutical drugs.

6 General Discussion

The use of Activated Carbon as a pharmaceutical drug adsorbent is a reliable method to immobilise pharmaceutical drugs. The process is quick, effective, and unavailable and unusable for all practical purposes.

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