

Recent developments in the use of activated charcoal in medicine

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ABSTRACT

One of the raw forms of graphite is activated charcoal which has an extensive surface area allowing for the adsorption of a wide range of chemicals. It possesses the strongest physical adsorption forces of the available materials, as well as the largest volume of adsorbing porosity. Activated charcoal acts as an adsorbent, collecting and storing substances in the gastrointestinal tract, reducing or blocking absorption in the bloodstream. The ingested toxins interact with charcoal by recycling toxins in the intestinal cavity. In cases where the drug has not been absorbed from the abdominal system, it is recirculated through the liver and intestines or by means of passive diffusion or active secretion. The article aims to review the most recent advances in the use of the activated charcoal, including the dose, how charcoal acts in the body, the mechanism of action, administration, contraindications, as well as the impact of various factors on the adsorption process. In addition, we also discussed numerous medical applications of activated charcoal.

Introduction

Activated charcoal is a porous carbonaceous adsorbent in which the crystalline structure is damaged in the course of production, resulting in the formation of unstable and inhomogeneous pores in terms of energy and activity [1]. These pores are usually located on the outer surfaces of activated charcoal, although they can also be found inside. In terms of adsorption capacity, activated carbon has a larger capacity than any other adsorbent, and its surface area fluctuates from 300 m²/g to 5000 m²/g [2].

It is possible to distinguish two types of activated charcoal, i.e. powdered and granular. In comparison with carbons with larger particle sizes, powdered, micron-sized activated charcoal particles are milled from millimeter-sized granular activated charcoal, and demonstrate faster kinetics as well as a greater capacity for contaminants removal. The particle size of granular activated carbons generally ranges between 0.2 mm to 5 mm; moreover, it provides clean handling and tends to last longer than powder form [3]. Carbonization of the raw material is the first step in the production of activated charcoal, in which

thermal decomposition occurs in the absence of air. The majority of the hydrocarbons are first eliminated as gases during carbonization, without the use of chemical agents, in a process known as pyrolytic decomposition, also referred to as destructive distillation. In the course of the process, when coal is heated, chemical changes occur which result in the evaporation of gases and condensable vapors, thus, leaving a solid residue consisting almost entirely of carbon. The bituminous coal softens during this process, fuses and resolidifies to form coke, a porous substance rich in carbon. The carbonized products formed in this manner typically exhibit only a low adsorption capacity due to their underdeveloped pore structure and small surface area. This, in turn, improves in the process of activation, which converts the carbonized raw material into a form having the greatest number of scattered pores of various shapes and sizes, and producing a large and rich surface product [4–6]. The activation process can be performed chemically or physically. Chemical activation is the process of impregnating the precursor substance with dehydrating materials, such as NaOH, KOH, ZnCl₂, K₂CO₃, and H₃PO₄, to affect the pyrolytic decomposition of the precursor material, reduce the activation temperature, and prevent the production of tar. Physical activation includes partial gasification of the carbonaceous material at high temperatures in an inert ambient, followed by activation with oxidizing gases, such as CO₂, steam, air, or a mix of these [7, 8].

Since activated charcoal has been widely used, a number of sources have been involved in its preparation, which comprise nutshells [9–11], apricot stones [12], pistachio-nut shells [13, 14], agriculture waste [15, 16], almond shells [17], palm shell [18], wood apple fruit shell [19], sorghum waste [20], coir pith [21], olive stones [22], rubber tree [23], tea waste [24], and cotton stalk [25]. Furthermore, it has been also prepared from hair [26], bovine horns [27], waste tires [28], and several other sources. Several methods have been involved in the modification of activated charcoal to increase its surface area and enhance its adsorption properties. These methods include treating the material with different chemicals suitable for this purpose, e.g. citric acid [29], K₂CO₃ [30], KMnO₄ [31], ZnCl₂ [32], O₃ [33], H₂O₂ [34], H₃PO₄ [35], and NaOH [36]. The review aims to

describe the recent medicinal uses and the benefits of activated charcoal application.

Dose of Activated Charcoal

Activated charcoal does not have any absolute recommendations for its use [37]. A single dose for adults is 10 times the weight of the toxic substance ingested, up to maximum of 100 grams. Numerous studies aiming to test the ability of activated charcoal to slow absorption with various charcoal-to-toxin ratios established a carbon-to-drug ratio of 10:1 [38]. Additionally, in order to test the efficacy of activated charcoal:drug ratios of 1:1, 2:1, 4:1, and 8:1 a rat model was involved for phenobarbital, chloroquine, and isoniazid exposures. At 1:1 ratios, absorption was reduced by 7%, 20%, and 1.2%, respectively, while at 8:1 ratios, absorption was reduced by 89%, 96%, and 80% [39]. Multiple dosages of activated charcoal have been effective in various circumstances, which may be helpful in the removal of a wide range of drugs [40–44]. The process includes two or more doses of activated charcoal in a row for the effective toxin removal. Administering multiple doses increases the excretion rate of a drug which has already been absorbed. In fact, this process removes drugs which are subject to significant entero-hepatic reabsorption, or exhibit a high affinity for charcoal and can be transported through the intestinal-capillary junction to be further absorbed. A study on the removal of fexofenadine by activated charcoal indicated that the amounts of the drug adsorbed following a repeated dose of activated charcoal increased by about 70% [45]. Aspirin, carbamazepine, dapsone, cyclosporine, dextropropoxyphene, digoxin, digitoxin, meprobamate, nadolol, nortriptyline, phenobarbitone, phenytoin, piroxicam, valproate, sotalol, and theophylline are all improved by the repeated treatment with oral activated charcoal. In severe poisonings, repeated dosing with oral activated charcoal appears to be necessary until the patient's condition have improved, or up to the point where plasma concentrations have dropped to the non-toxic levels. Activated charcoal doses of 20 to 50 g dissolved in water are usually administered every 4 to 6 hours for 1 to 2 days. Constipation is not a frequent adverse reaction, however, laxatives, such as sorbitol or lactulose, can be used in conjunction with

Table 1. Chemicals in which multiple doses of activated charcoal improve clearance

Chemicals names	
Amitriptyline	Nadolol
Carbamazepine	Phenobarbital
Cyclosporine	Phenylbutazone
Dapsone	Phenytoin
Dextropropoxyphene	Piroxicam
Digitoxin	Propoxyphene
Digoxin	Quinine
Disopyramide	Quinine Sotalol
Theophylline	

charcoal [38]. A 50–100 g initial dose followed by 30–50 g supportive doses every 2–6 hours is a suitable protocol [46]. Maintenance doses from charcoal in the intestines adsorb the toxin once it has been released back into the bowels, preventing a delayed peak in serum levels [47]. Some chemicals in which their clearance is increased by multiple doses are shown in **Table 1** [48].

Mechanism of Action

Activated charcoal acts as an adsorbent, which captures chemicals in the gastrointestinal (GI) system and subsequently retains them within the charcoal, thus, decreasing or preventing them from being absorbed into the bloodstream [37, 49, 50]. Orally given activated charcoal does not undergo absorption through the intestinal lumen and acts in its unaltered form within the gastrointestinal tract. If the drug has not been absorbed at this location, the ingested toxins interact with charcoal by recirculating the toxins into the intestinal lumen by either enterohepatic recirculation or entero-enteric recirculation through passive diffusion or active secretion [51]. The activated charcoal adsorptive surface comprises a variety of chemical forms, including carbonyl and hydroxyl groups that adsorb toxic chemicals with varying affinities [52]. Moreover, particle size, pore size, surface area, solubility, temperature, pH, the presence of inorganic ions, and other factors, have all been shown to alter its adsorptive activity in vitro [53]. Activated carbon adsorbs toxins in their non-ionized forms to a better extent, whereas adsorption is less common in polar, water-soluble compounds. Due to its pharmacodynamics, activated charcoal is most effective in adsorbing non-polar, poorly water-soluble organic toxins best [54].

Administration

When ingested poison is still present in the gastrointestinal tract, and when it is thought that the benefits of avoiding toxin absorption outweigh the dangers of providing activated charcoal, the patient should be administered a charcoal dose. Activated charcoal can be provided orally, or by means of nasogastric and orogastric tubes [55]. Activated charcoal is available as carbon tablets, powder, or granulate. Powder or granular activated charcoal, where the doses ranging from 10 to 100 g, appears to be more feasible in clinical practice. In contrast, carbon tablets, only contain 250 mg of carbon, therefore, a significant number of tablets would be necessary to generate an acceptable carbon surplus. Any liquid can be used to suspend activated charcoal in, although water is the preferred medium [56].

Risks of Use

Activated charcoal has long been thought to be safe in the treatment of poisonings; however, this assumption, is currently being questioned [57]. Vomiting, corneal abrasions, and lung aspiration comprise the risks associated with single-dose activated charcoal delivery. Despite a few caveats to using activated charcoal, it still remains a good treatment option [58]. The most significant consequence following the activated charcoal administration is pulmonary aspiration [50]. Aspiration occurs when a nasogastric tube is accidentally inserted into the trachea instead of the stomach [59, 60]. Regardless of whether activated charcoal is present, gastric content aspiration may lead to severe airway obstruction, bronchospasm, hypoxemia, and pneumonia [61]. In addition, according to one of the studies, a charcoal-containing empyema developed in one patient [62]. It is vital to bear in mind that intubation for an extended period of time, death [50], and permanent lung injury [63] all constitute the possible negative outcomes. Activated charcoal should only be administered to cooperating patients, since. In terms of not fully conscious patients, the administration is not recommended, since the swallowing reflexes are impaired and there is a considerable risk of aspiration. In acute intoxication, intubation is required in order to secure the airways prior to

activated charcoal administration through a gastric tube [56]. Other contradictions involve the cerebral seizures risk and dysphagia [64].

Combination with Laxatives

Over the years, a common practice was a simultaneous administration of a laxative, such as sodium sulfate at the same time; nevertheless, this is no longer recommended. In certain situations, a laxative may be given following the ingestion of a medication reducing gastrointestinal movement activity. This is also a frequent method in the case of constipation, which may be followed with a dose of a bowel stimulant. If polyethylene glycol electrolyte solution and activated charcoal were given at the same time, the substances would bind together, limiting the adsorption capacity, therefore, they are administered individually (usually at two-hour intervals) [56, 65]. The sweetener and laxative agent, sorbitol, has been linked to emesis [37].

Effect of pH

The adsorption capacity of activated charcoal is affected by the pH of the environment. Drugs are most effectively adsorbed on activated charcoal in their undissociated form, whereas acids demonstrate greatest adsorption at low pH and bases at high pH [66]. In fact, it was found that the pH has a clear effect on the adsorption of aspirin [67], caffeine [68], paracetamol [69, 70], acetaminopirid pesticide [71], carbendazim and linuron [72], methylparaben [73], and many other compounds.

Effect of Time

The antidotal efficacy of oral activated charcoal is undoubtedly affected by delaying delivery after drug ingestion. As a result, it should be supplied as soon as possible [38]. The delay in administering activated charcoal and the amount given is the most critical determinants of its efficacy in acute poisonings. Activated charcoal should be given as a water suspension as soon as possible following toxic substance ingestion, preferably within 30 minutes [74].

Effect of Gastrointestinal Content

Similarly to any other competing solute, gastrointestinal contents are likely to affect drugs adsorption on activated charcoal. Although the presence of food in the stomach of individuals suffering from drug overdoses reduces activated charcoal adsorption capacity, it allows charcoal to be effective for a longer period [75].

Types of Adsorbed Drugs

A variety of drugs, phytotoxins, and dangerous compounds bind onto the activated charcoal surfaces, inhibiting their absorption through the gastrointestinal tract. In fact, it stops a potential enterohepatic and/or enteroenteric circulation as a secondary decontamination mechanism. The ability of activated charcoal to attach to the harmful chemical is determined by several parameters, including solubility, polarity, and ionization of the substance [76]. Non-dissociating compounds, such as mercuric chloride and iodine, are well adsorbed, although strongly dissociated salts, e.g. NaCl or KNO₃, are poorly adsorbed. Large, poorly water-soluble organic molecules, such as fatty acids, are more effectively adsorbed on activated charcoal than smaller molecules with polar substituent groups, as is the case of alcohols. Since pH may affect the process of ionization, salicylate is fully adsorbed at a low pH, when the drug is non-ionized, although the opposite is true in the case of basic compounds, such as aniline [77]. **Tables 2, 3, and 4** list compounds which, due to their physicochemical properties, undergo adsorption, are insufficiently adsorbed or are not adsorbed at all by activated carbon [56].

Activated Charcoal for Chronic Kidney Disease Patients

Patients with various stages of renal diseases are administered different forms of activated charcoal which is accompanied by reduced protein diets in order to control uremic symptoms. These occur when urea as well as other urine toxins bind to activated charcoal and are excreted with feces, forming a concentration gradient which allows the toxins to continue to diffuse [78]. Fur-

Table 2. Substances that are adsorbed on activated charcoal

Substance names
Amphetamines
ACE inhibitors
Antidepressants (except lithium)
Antiepileptics
Antihistamines
Aspirin salicylates
Atropine
Beta-blockers
Benzodiazepines (NB: somnolence)
Barbiturates
Quinine quinidine
Calcium-channel blockers
Dapsone
Chloroquine and primaquine
Digoxin
Digitoxin
Neuroleptics
Non-steroidal antirheumatics (NSAR)
Diuretics (especially furosemide torasemide)
Oral antidiabetics (especially glibenclamide glipizide)
Opiates dextromethorphan (NB: somnolence)
Paracetamol
Piroxicam
Tetracyclines
Theophylline

Table 3. Toxins that are adsorbed on activated charcoal

Toxin names
Amatoxin (death cap)
Aconitine (aconite)
Colchicine (autumn crocus)
Cucurbitacin (courgette, Cucurbitaceae)
Ergotamine, ergot alkaloids
Ibotenic acid, muscarine (fly agaric, panther cap)
Nicotine (tobacco)
Ricin (castor oil plant)
Strychnine (nux vomica)
Taxanes (yew)
Digitalis glycosides (foxglove)

Table 4. Substances that are insufficiently adsorbed on activated charcoal or not at all

Substance names
Alcohols (e.g., ethanol, methanol, and glycols [e.g., ethyleneglycol])
Inorganic salts (e.g., sodium chloride)
Metals and their inorganic compounds (e.g., lithium, iron, or other heavy metals [for instance lead or mercury])
Organic solvents (e.g., acetone, dimethylsulfoxide)
Acids and bases
Cyanides

thermore, other studies have shown that sorbents can help dialysis by removing waste products, such as urea, indoxyl sulfate, other urinary toxins, thereby improving the dialysis process [79].

Hypercholesterolemia Treatment

The studies demonstrated that activated charcoal is efficient in decreasing cholesterol levels. In one of the studies, seven patients with hypercholesterolemia were administered 8 g of activated charcoal three times daily for four weeks. Following this period, total cholesterol and Low-Density Lipoprotein-cholesterol levels in the blood were reduced by 25% and 41%, respectively [80]. In a three-week cross-over research,

seven patients were administered charcoal at 4, 8, 16, or 32 grams per day, followed by bran. In a dose-dependent way, charcoal reduced the total and Low-Density Lipoprotein-cholesterol in the blood (maximum 29 and 41%, respectively) while increasing the High-Density Lipoprotein/Low-Density Lipoprotein cholesterol ratio (maximum 121%). Ten more patients with severe hypercholesterolemia were administered activated charcoal 16 g, cholestyramine 16 g, activated charcoal 8 g plus cholestyramine 8 g, or bran daily for three weeks in a random order. The Low-Density Lipoprotein-cholesterol total concentrations were reduced by charcoal (23% and 29%, respectively), cholestyramine (31% and 39%), and their combination (30% and 38%). Activated charcoal, cholestyramine, and their combi-

nation enhanced the High-Density Lipoprotein/Low-Density Lipoprotein ratio from 0.13 to 0.23, 0.29, and 0.25, respectively [81].

Preventing Gas and Bloating

The evidence with regard to the effectiveness of activated charcoal in decreasing lower intestine gas and symptoms is conflicting. A double-blind clinical investigation was conducted which included two population study groups: in the United States (n = 30) and in India (n = 69), which were different in terms of eating habits as well as gut flora ecology. Breath hydrogen levels were tested using lactulose as the substrate to quantify the quantity of gas produced in the colon. In both groups, activated charcoal significantly decreased hydrogen levels in the breath and considerably reduced symptoms of bloating and stomach cramps resulting from gaseousness in both groups [82]. After consuming a gas-producing meal, the effectiveness of activated charcoal in treating intestinal gas was investigated. The number of flatus occurrences, as well as the levels of hydrogen in the breath, were also counted. Orally administered activated charcoal was found to be effective in preventing the substantial increase in the frequency of flatulence, and elevated breath hydrogen concentrations which occurred following gas-producing meals in these studies [83]. Moreover, the capacity of activated charcoal to suppress intestinal gas production was tested in vitro, as well as in vivo. Human fecal homogenates were involved in the in vitro investigations, which were incubated with or without extra carbohydrates. In all of the trials, the activated charcoal treated homogenate produced and consumed hydrogen, as well as carbon dioxide at similar rates as the untreated control group. Following a baked beans meal, a double-blind assessment of hydrogen and flatus excretion was used to investigate the effect of activated charcoal on gas generation in vivo. In patients who were administered 16 capsules of activated charcoal (4 g) vs. the placebo, no significant difference was observed in breath hydrogen content or in the occurrence of flatulence. In vitro and in vivo tests revealed that activated charcoal did not affect gas production [84]. Furthermore, the fecal release of intestinal gases was assessed prior to and following the charcoal treatment in five healthy individ-

uals who voluntarily ingested 0.52 g of activated charcoal four times per day for the period of one week. Additional investigations were conducted in vitro aiming to compare the binding capability of charcoal to the sulfur gas generated by feces which would account for the in vivo results. According to the study results, activated charcoal ingestion did not cause a substantial reduction in the fecal discharge of any sulfur-containing gases, nor did it affect the total fecal gas release, or abdominal discomfort. In fact, as the in vitro investigations indicate, inability of the ingested activated charcoal to inhibit sulfur gas escape may stem from the saturation of binding sites of activated charcoal during passage through the intestine [85].

Reducing Body Odor

The potential of activated charcoal in wound treatment is related to its ability to adsorb gases. Activated charcoal is increasingly used to control smell, and it is particularly helpful in the treatment of fungating lesions [86]. The statistical study revealed that employing activated charcoal alone or in combination with soda-bicarbonate significantly reduced the odor. The study suggested using activated charcoal with or without soda bicarbonate as a cost-effective method to decrease the unpleasant odor accompanying severe skin loss [87]. Interestingly, activated charcoal was found to reduce the malodor of flatus in dogs by modifying the generation or availability of hydrogen sulfide in the large intestine, according to a study [88]. Leg ulcers are usually accompanied by odor, thus, reducing odor constitutes an adequate therapy. It was observed that activated charcoal dressing for malodor helped two individuals suffering from leg ulcers [89]. In addition, activated charcoal lowers healing time and eliminates bacterial barriers, according to an exploratory clinical trial aimed at determining the efficacy of an activated charcoal silver dressing in reducing the number of bacteria in chronic wounds with no clinical symptoms of local infection [90].

Treating Wounds

Zorflex is a brand-new antibacterial dressing composed entirely of activated charcoal fabric.

It draws bacteria to the surface and binds them there, thus allowing their removal when the dressings are changed. No known side effects have been demonstrated and, therefore, such dressings can be used for short, or extended periods of time. The activated charcoal cloth treatment was used to treat patients suffering from severe chronic venous leg ulcers, prone to recur in four case studies [91]. Clinical evidence suggests that employing activated charcoal impregnated with silver in the course of chronic wounds treatment, even at the debridement stage, could be beneficial. This process may be helpful in the removal of fluids and toxic substances which delay healing [92].

Use as Dentifrices

Toothpastes with activated charcoal are gaining popularity, despite the lack of evidence in terms of their safety in individuals with erosive tooth wear. Nevertheless, the use of such toothpastes did not put these persons at any greater risk [93]. Moreover, in a study regarding tooth decay, activated charcoal was found to be a deterrent to dental caries [94]. Activated charcoal toothpaste and powders are popular oral hygiene solutions for brushing teeth and removing extrinsic stains, and are thought to become more commonly used in various countries worldwide [95]. In fact, the charcoal-containing dentifrices were abrasive within permitted limits set by the ISO and did not adsorb fluoride [96]. However, another study indicated that the use of an activated charcoal-based product, described as a natural whitening agent, before brushing teeth with toothpaste is not only ineffective in terms of changing the color of the teeth, but may also result in enamel surface changes [97]. According to a recent review study, data to support the claim that charcoal and charcoal-based dentifrices are safe and effective are inadequate [98].

Conclusions

Adsorbents play a vital role in removing the effects of poisoning due to an overdose of drugs. One of such adsorbents, commonly used in the medical field, is activated charcoal. It has a substantial surface area, which renders it to be an effective adsorbent, it is also inexpensive and

can be obtained from a variety of sources. Activated charcoal has a wide range of medical applications extending beyond the treatment of poisoning. It is used for hypercholesterolemia, in gas and bloating prevention, reducing body odor, treating wounds, as well as in dentifrices.

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Conflict of interest statement

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