

Venetian treacle and the foundation of medicines regulation

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Mithridatium and the related product Theriac were both regarded from the time of their original formulations in the 2nd Century BC and the 1st Century AD respectively, until the mid 18th Century as universal panaceas. Any failure of these products to achieve the desired therapeutic result was attributed to defective composition or manufacture. As a result measures were introduced to ensure the quality of ingredients used in these products composition, the establishment of standard formulations and assurance of the competence of the manufacturer. Manufacture frequently was required to take place in public.

Doubts about the efficacy of these panaceas arose in the mid 18th century and concerns of the adverse nature of interactions between the numerous ingredients surfaced in Heberden's treatise of 1745, as result of which these products disappeared from Editions of The London Pharmacopoeia after 1746. Subsequently, arising from these concerns for safety and efficacy, a call was made in 1799 for the establishment of a Public Committee of eminent physicians to scrutinise all new products prior to their launch to an gullible public. The concepts developed in the history of Mithridatium form the basis of modern medicines regulation.

Introduction: classical origins of Mithridatium and Theriac

Mithridates VI, King of Pontus came to the throne in 120 BC as a 13-year-old boy [1]. Pontus abounded in medicinal plants and Mithridates acquired considerable knowledge of them. Like every despot of that period, Mithridates lived in fear of being assassinated by poisoning, in consequence of which he sought the universal antidote to all poisons. Mithridates proceeded along a simple line of reasoning. Having investigated the powers of a number of single ingredients, which he found to be the antidote to various venoms and poisons individually, he evaluated them experimentally on condemned criminals. He then compounded all the effective substances into one antidote, hoping thereby to produce a universal protection. A daily dose was taken prophylactically to give the immunity he sought.

Galen [2], writing in the second century AD at a time when he was physician to the Roman Emperor Marcus Aurelius, refers to 'Mithridatium' and a formulation

derived from it by one Andromachus, Nero's physician. It is said that Andromachus removed some ingredients from Mithridates' formulation and added others, particularly viper's flesh. To this new product he gave the name 'Galene', which means 'tranquillity'. Galene became known as a theriac. Details of various theriacs, including Mithridatium and Galene, were given in Galen's Antidotes 1 and Antidotes 11. According to Galen, Mithridatium contained 41 ingredients and the Galene of Andromachus 55 components.

The preparation of Galene was simple in that its ingredients were free of fractional measures. Four vipers cut down small were placed in a solution of sal ammoniac, about one gallon, to which were added nine specified herbs and Attic wine, together with five fresh squills also cut down small. The pot was covered with clay and set upon a fire. When the vapour came out of the four small holes left in the clay seal, dark and turgid, the heat had reached the vipers and they were cooked. The pot was left to cool for a night and day. The

roasted matter was taken out and pounded until all was reduced to powder. After 10 days the powder was ready for the next stage of manufacture.

At the final stage the prescribed quantities of 55 herbs previously prepared by various processes, along with the prescribed quantity of squill and viper flesh powder (48 drachms), were added to hedygium, long pepper and poppy juice (all at 24 drachms); eight herbs including cinnamon and opobalsam (all at 12 drachms); 18 herbs including myrrh, black and white pepper and turpentine resin (at 6 drachms); 22 others and then Lemnian earth and roasted copper (at 4 drachms each); bitumen and castoreum (the secretion of beaver); 150 drachms of honey and 80 drachms of vetch meal.

The concoction took some 40 days to prepare, after which the process of maturation began. Twelve years was considered by Galen the proper period to keep it before use. Galen records that the Emperor Marcus Aurelius consumed the preparation within 2 months of its being compounded without ill effect.

Mithridatium was similar but contained fewer ingredients and no viper, but did contain lizard! The other differences were that the opium content of Andromachus' theriac was higher than that of Mithridatium, which also differed in containing no Lemnian earth, copper or bitumen and 14 fewer herbal ingredients.

Both Mithridatium and Galene were taken orally with water or wine, but were also used topically on the skin or even in the eye. The theriac, Galene, was also used by Galen to treat quartan fever (malaria), which was prevalent in the Pontine Marshes near Rome. Aetius (first century AD) stated that beyond question the best remedy for venomous bites was theriac of Andromachus applied as a plaster [2].

Mithridatium re-entered western medicine culture by two routes. The first was directly from Byzantine or other eastern sources, for example a Saxon leechbook of the 11th century records that Abel the Patriarch of Jerusalem sent Mithridatium or theriac to King Alfred the Great, who died on 26 October 899 [3].

The *Leechbook of Bald* [4] is the most important piece of medical literature to have survived from the Saxon period. The document is in two parts or leechbooks, the first containing 88 chapters and the second 67 chapters. They were written approximately 900–950 from an earlier 9th century Latin text. A verse at the end of the second leechbook suggests that these books belonged to a physician or leech called Bald, and were written down by a scribe called Cild. The most important passage is contained in the second leechbook and concerns King Alfred. It refers to his request that the Patriarch Elias of Jerusalem send him remedies which the prelate had

found to be effective. A theriac formulation appears in this leechbook [5].

The second route was when the works of the Greek and Roman medical writers again became available in Italy, possibly via Arabian influences in Spain or through the University at Salerno. Theriac appears to have been more greatly favoured than Mithridatium as a remedy for poisons. In the 12th century, theriac was being manufactured in Venice and widely exported. In England it became known as Venetian treacle ('treacle' is a corruption of theriac). Theriac became an article of commerce, with Venice, Padua, Milan, Genoa, Bologna, Constantinople and Cairo all competing. The manufacture of these theriacs took place in public, with much pomp and ceremony.

It was commonly thought by those in authority that if Mithridatium or theriac did not produce the desired cure, this was due to incorrect preparation (perhaps with adulterated or poor-quality materials) or to incorrect storage after use. As the only cause for therapeutic failure therefore lay with the pharmacist who compounded the mixture, the remedy lay in careful scrutiny of manufacture, which should be in public. Any misdemeanour would then be detected and immediately published [6–9] (see Figures 1 and 2).

Confusion of names

Mithridatium is consistently so referred to, but Theriac Andromachus is referred to as Galene, Venetian treacle, and after the publication of the *London Pharmacopoeia* as London treacle or occasionally as Treacle, and by other names based on its place of manufacture. For example, Sir John Paston acquired some pots of Genoa treacle in 1466 from an apothecary who swore that they had never been opened since they left Genoa [10].

Nicholas Culpeper [11], in his *Dispensatory* (1649), refers to both Mithridatium and Venetian treacle. References in English literature to theriac frequently refer to it as treacle. For example, Miles Coverdale translated balm as treacle in his Bible of 1538. This was repeated in the Matthew Bible and Bishops' Bible of 1568. Jeremiah 8 v. 22 therefore read: 'Is there no treacle in Gilead? Is there no physician there?'

Concepts of inspection of manufacture of medicines by apothecaries in the charters of the College of Physicians

As early as 1423 the 'Commonality of Physicians and Surgeons of London' appointed two apothecaries to inspect the shops of their colleagues and bring any who offended in the quality of their wares before the Mayor and Aldermen of the City of London.



Figure 1
Apothecary being chastised by physicians from a 13th century Arabic manuscript

The College of Physicians was founded in 1518 by Henry VIII, and in 1540 was passed one of the earliest statutes on the control of drugs [12] (32 Henry VIII c 40 for Physicians and their Privileges), which empowered the physicians to appoint four inspectors of ‘Apothecary Wares, Drugs and Stuffs’ (see Figure 3). Section 2 of the Act gave the physicians the right to search apothecaries’ shops for faulty wares with the assistance of the ‘Wardens of the said mystery of Apothecaries within the said City’. If the search showed drugs that were ‘defective, corrupted and not meet nor convenient to be ministered in any medicines for the health of man’s body’, the searchers were to call for the Warden of the Apothecaries and the defective wares were to be burnt or otherwise destroyed.

This Act was incorrect in defining the apothecaries as a separate body – they were at this time members of The Grocers’ Company. This was corrected in the reign of Queen Mary by an Act of 1553 (1 Mary sess 2 c 9) [13]



Figure 2
The public preparation of theriac from *Das Neuwe Distillier Buch*, Strasbourg 1531

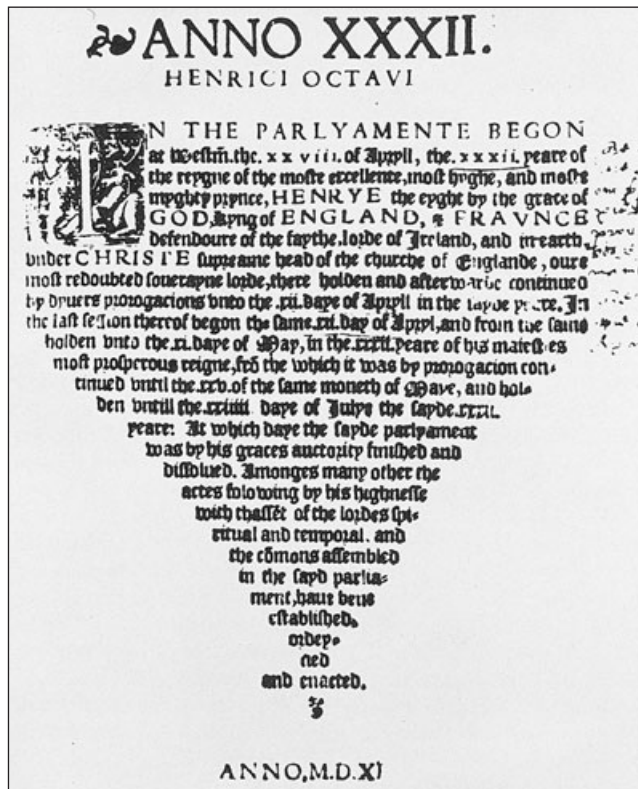


Figure 3
The title page of ‘The Pharmacy Wares Drugs and Stuffs Act 1540’ (32 Henry VIII c 40)

in which it was enacted ‘. . . for the better execution of the search and view of Poticarye Wares and Drugges and Compositions according to the tenour of a statute made in the Two and Thirtieth yeare of the Reigne of the said late King Henry Eighth that it shall be lawfull for the Wardeins of the Grocers or one of them to go with the say’d Physitions in their view and searche’.

It is revealing that whereas the penalty for refusing to have wares examined was 100 shillings in Henry’s day (of which he took half), by Mary’s day this had been raised to £10. The wording of the Act was also changed slightly, in that under Henry the Wardens were to be called for, but under Mary they had to go.

Henry was also determined that the 1540 Statute would be obeyed and an errant apothecary punished and not allowed to make excuses: ‘. . . in the Kings Court . . . no wager of law, esoin (excuse) or protection shall be alloweth . . . apothecaries to sell or prescribe any poisonous substance or drug . . . to the body of any man, woman or child save on the written prescription of a physician or upon a note in writing from the purchaser’.

The making of theriac and Mithridatium was made subject to supervision under the Pharmacy Wares, Drugs and Stuffs Act of 1540. In the reign of Elizabeth I the making of theriac was entrusted only to William Besse, an apothecary in Poultry, London. He had to show the finished product to the Royal College of Physicians (*vide infra*).

Records of these early inspections do not exist – the Library of the Royal College of Physicians of London in Warwick Lane was largely destroyed by the Fire of London in 1666, only 140 volumes being saved including several volumes of the *Annals of the College*. From these Annals Clark has distilled this account [14].

On the day of a visitation of apothecaries 20 July 1586, The Master and Wardens were concerned at the sale of a treacle called ‘Jeane Triacle’ (Genoa treacle) which they found to be unwholesome for adults and children, being indeed compounded by certain rude and unskilful men. Moved by Christian charity to all good people, they besought the College to set down a ‘receipt’ for the true composition of this treacle, which should be registered at Grocers Hall. Anyone who was admitted to make it should take such an oath as the College might direct. The letter was delivered by one apothecary, William Besse, and the College beadle was sent to deliver the College’s recipe put down upon ‘mature deliberation and consent’ to Besse, the only apothecary approved to make Mithridatium.

The Apothecaries’ intent was to stimulate The College of Physicians to produce a pharmacopoeia for use by the apothecaries and perhaps relieve the indig-

nity of inspection, but the result was a further restriction to a single apothecary permitted to manufacture Mithridatium.

On 8 October 1617 the College obtained a new Charter from King James I [15]. The new Charter was all the College could have wished. It named Drs Atkins [16], Mayerne and Lister as the petitioners; confirmed the existing powers of the College; gave it the right to sue for all penalties inflicted by it and to retain the King’s share for its own use without rendering any account; and gave the President and censors the right to examine, survey, govern, correct and punish all physicians, practitioners of physic, apothecaries, druggists in the City of London [15].

A further Charter of James II of the ‘Eleaventh day of March in the Third Year of His Reigne (1688) did grant unto the said President Fellowes or Commonality divers liberties and privileges and immunities powers abilities and authorities as well as powers to prevent the great abuses frauds enormities frequently practized and comitted by divers apothecaries druggists and others in the said city of London and to punish and suppressse all ignorant and unpractised empiricells who have in open defyance and contempt of authority dared publickly to professe and practize physick’ [17].

Pharmacopoeias set standards for the manufacture of Mithridatium and Theriac

Another technique to control the quality of drugs is the issue of a pharmacopoeia (Greek ‘pharmakon’, a drug, ‘poiia’, making). The official and obligatory guide for the apothecaries of Florence was published in 1498 and is generally regarded as the first official pharmacopoeia in Europe in the modern sense, i.e. of a specific political unit.

Other cities soon followed in the publication of obligatory formularies, e.g. Barcelona in 1535 (*Concordia Pharmacolorum Barcinonesium*) and Nuremberg in 1546 (*Dispensatorium valerii Cordis*).

In England it was not until Elizabethan times that it became obvious that there was a need for such a pharmacopoeia or formulary. This was first considered by the College of Physicians in 1585. However, work proceeded very slowly and the *Pharmacopoeia Londinensis* was not published until 1618 (see Figure 4). There were two issues: one on 7 May and the first ‘official’ edition on 7 December. This latter was by no means a reprint of the earlier one and was substantially enlarged and changed [18].

In 1607 James I agreed to grant a Charter to the Grocers, who recognized the Apothecaries as a separate group. Ten years later in 1617, James I gave the Apoth-

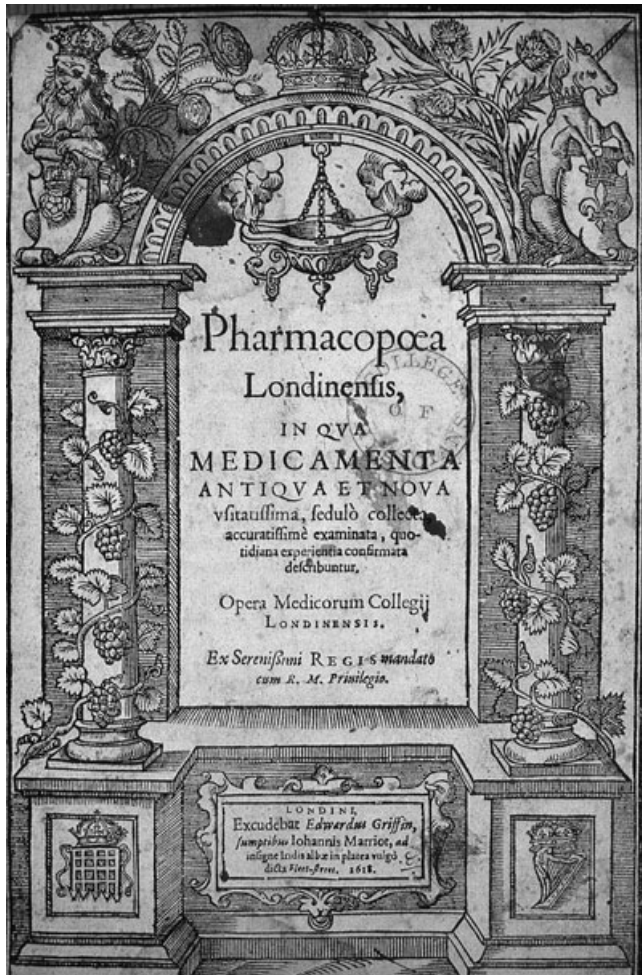


Figure 4

Title page of the *London Pharmacopoeia* 1618

ecaries a Charter to separate them from the Grocers as ‘The Worshipful Society of the Art and Mistery of Apothecaries’ [19]. King James’ proclamation on the Apothecaries Charter in 1617 included reference to another proclamation which had preceded it by 2 years. This announced that a book entitled *Pharmacopoeia Londinensis* had been compiled by the College of Physicians at the King’s command and was ready for press. ‘No one throughout the whole of England was to compound any medicine, or distil any oil or waters or extractions named in it except in the manner therein prescribed, unless specially ordered by some learned physician. No one not a member of the Apothecaries’ Company was to sell any composition named in the book or any medicine within London or seven miles about it’ [20]. The reference to the *Pharmacopoeia* in the Apothecaries Charter preceded its publication by nearly 18 months! [18].

Other editions of the *Pharmacopoeia Londinensis* appeared in 1650, 1677, 1721, 1746, 1788. A 10th Edition appeared in 1850, the last before the *British Pharmacopoeia*.

Mithridatium, Galene and treacle used for the treatment of plague

The publication of the *London Pharmacopoeia* in December 1618 [18] setting out detailed formulations of theriac and Mithridatium had made supervision easier, and manufacture was clearly no longer entrusted to a single apothecary, as was demonstrated in the London plague of 1625 when three apothecaries were approved to make 160 lb, 50 lb and 40 lb of Mithridatium.

In 1665 the Great Plague of London broke out and Charles II turned to the Royal College of Physicians for advice. It was eventually published as: ‘Advice set down by the College of Physicians (at the Kings Command) containing certain necessary directions for the cure of the Plague and preventing infection’ [21] (see Figure 5). The streets were to be kept clean and flushed with water in order to purify the air, fires were to be lit in streets and houses, and the burning of certain aromatic materials such as resin, tar, turpentine, juniper, cedar and brimstone was enjoined. The use of perfumes on the person was recommended. Special physicians attended by apothecaries and surgeons were appointed to carry this out. The main internal remedies that were recommended for the plague were London treacle, Mithridatium, Galene and diascordium, a confection prepared from water germander. Victims of the plague who developed buboes were treated with a plaster of either Mithridatium or Galene applied hot thrice daily.

This pamphlet was well circulated, and is referred to by Daniel Defoe in *Journal of the Plague Year* published in 1722, who states ‘The direction of the physicians was done by a consultation of the whole College’ [22].

Inspection in the 18th century extended to all manufacturers

In December 1720 The College of Physicians of London approved the President’s draft of a petition to Parliament regarding the difficulties which the servants of the College met when they collected, at the place of execution, corpses of malefactors to which their Elizabethan Charter gave them a right. On 25 June 1723 Sir Hans Sloane, as President, proposed that a Bill should be promoted to make the procuring of bodies easier; but the College was then led by the President and Censors to combine this with clauses about searching apothecaries’ shops. The Bill was drafted by Mr Mead, the College attorney, who worked in the new point that the censors were empow-

Certain necessary
DIRECTIONS
 As well
For the Cure
 OF THE
PLAGUE,
 As for preventing the
INFECTION:
 WITH
Many easie Medicines of small Charge,
 very profitable to His Majesties Subjects.
Set down by the Colledge of Physicians.

By the Kings Majesties Special Command.

LONDON,
 Printed by *John Bill and Christopher*
Barker, Printers to the Kings most
 Excellent Majesty. 1665.

Figure 5

'Certain necessary directions as well for the cure of the Plague', 1665

ered to search shops of all persons selling medicines, as they already did for apothecaries' shops and the right of search was to be extended from the City of London, to which it had hitherto been confined, to an area of 7 miles radius around the City. Various attempts were made to insert other clauses to the Bill. The Apothecaries wished to require that the concurrence of the Apothecaries would be necessary before any medicines were destroyed. Other attempts to exempt warehouses from the search were unsuccessful. However, all medicines made by virtue of letters patent were exempted. This exemption was made because of a clause submitted by a Licenciate of the College, Dr Joseph Eaton, who had patented a styptic and who wished it to be exempt from search. Another clause exempted any Physician from search. The physicians' self-interest thrived!

The Bill became Law in April 1724 as 10 Geo 10 c 20, but strangely the original purpose of the Bill, i.e. procurement of corpses for dissection, was lost [23].

Records of 'visitations' of apothecaries shops and premises from which medicines were sold exist in The College Library for the years 1724–1754. It is clear from these records that the College Censors wasted no time in enforcing their new powers outside the City of London [24]. The following is a synopsis of their visitations over this period:

On 27 May 1724, 28 premises in the Strand, Pall Mall, St James, and German (Jermyn) Street were inspected. Mr James Goodwin of Haymarket was found to have manufactured Venetian treacle which was described as 'almost very indifferent – reprimanded'. The Censors were back on 7 June 1724 and several medicines condemned to be burnt in public before the doors of Mr Goodwin's shop. Goodwin had two shops, one in the City and the other in Haymarket – the latter was searched the second time in the owner's absence, two assistants being in charge. Goodwin claimed that the censors behaved with ferocious violence and had condemned five lots of his medicine including his stock of Venetian treacle. Mr Goodwin was not a Freeman of the Worshipful Society of Apothecaries and was clearly targeted by the College and the Society. Goodwin, however, took advantage of new appeal procedures, but at a special meeting of the full Comitia of the College the Fellows compared specimens of the condemned medicines with type-specimens from Apothecaries Hall and they upheld the decision of the Censors unanimously. A few days later the Censors destroyed the condemned medicines before his door, and continuing their visitation found and destroyed several more medicines.

James Goodwin nursed his grievance and made representation to the House of Lords in a pamphlet 'Brief for James Goodwin, Chymist and Apothecary, upon his Petition to the House of Lords' 1725, but his protests came to nothing.

The College Censors were diligent in their extended powers. On 22 June 1724 they conducted 15 visitations in the Borough, Southwark and London Bridge area and destroyed Venetian treacle confiscated from the shops of Mr Snaggs and Mr Thomas Pont. The visitations of 20 July 1724 record the inspection of 18 premises in the same area, eight of which belonged to surgeons. One of these surgeons, Mr J. Wood, was found to be in possession of defective Venetian treacle.

The 1724 Act was originally drafted to run for 3 years; its scope was extended in 1727 for a further 3 years. After 1731 the Act was not extended and the Censors had to operate within the terms of the Acts of Henry VIII and Mary I, but with their area of inspection extended beyond the City.

In the 30 years of visitation for which records exist

only two apothecaries raised objection to being inspected.

Also, Sir George Clark in his *History of the Royal College of Physicians of London* (1966) [25] records that The Worshipful Society of Apothecaries tested the strength of the College by a calculated defiance. Robert Gower, a train-band colonel, and Master for the second time, refused to show his medicines to the Censors. The College comitia of 1727 was informed and sought Counsel's opinion. No opinion has been found in the College archives, so no further light can be obtained from the Society's history [19]. The answer probably lies in the fact that the joint inspections by the College Censors and the Society's Wardens continued for another 150 years until these powers were revoked under the Food and Drugs legislation of 1872, although the last joint visitation had taken place in the 1850s. In the 10-year period 27 May 1724 to 30 July 1734, 791 shops were visited in the course of 37 inspection days, giving an average of 21 premises per day's inspection. In subsequent decades the College Censors were not quite so active (see Table 1).

On a typical visitation day, the four Censors of the College of Physicians and two Wardens of the Society of Apothecaries assembled at 10.00 h. After their round of inspections the group retired to a hostelry where at 16.00 h they sat down to dinner, at the College's expense, with The President, Registrar and Treasurer of The College of Physicians.

Inspections were as frequently commenting on products absent from premises as products that were defec-

tive. Products frequently reported as defective were Venetian treacle/Mithridatum/Theriac Andromachus, Tincture of Rhubarb, cinnamon, helleboris niger, absinth, aloes, jalop and, most frequently, Peruvian bark.

Three areas were noted where apothecaries' premises were most likely to be the source of problems. The Southwark/Borough/London Bridge, Whitechapel/Houndsditch/Aldgate and Clerkenwell areas seem to have figured large as areas of poor-quality shops. Surgeons' premises were frequently described as very bad, particularly in Southwark!

Mr Bevan's shop in Plough Court, the predecessor of Allen and Hanbury's (now part of Glaxo Smith Kline) [25] was singled out for very favourable comment on several inspections. For example, on 11 September 1728 it was described as 'extraordinary good'. The College of Physicians exerted their privilege to search apothecary shops up to the early 19th century. It is interesting to note that when the Censors visited Allen and Hanbury's (then William Allen and Co.) in the 1820s, they noted it was 'an excellent house' [26].

Antitherica 1745 – doubts on efficacy

The real attack on Mithridatum and Theriac was the 19-page pamphlet of William Heberden in 1745 [27] (see Figure 6). The pamphlet *Antitherica, Essay on Mithridatum and Theriac* was the first serious attempt to attack the efficacy of a product. William Heberden was well known not to mince his words [28, 29]. He refers to the 'injudiciousness, the ostentation and wantonness of this heap of drugs' and the mystique of manufacture – 'it still goes on to be prepared in the old manner as near as maybe in all the great cities of Europe'. Heberden concludes by appealing to the College of Physicians of London in flattering terms: 'Perhaps the glory of its (Mithridatum) first expulsion from a public dispensary was reserved to these times and to the English nation in which all parts of philosophy have been so much assisted in asserting their freedom from ancient fable and superstition, and whose College of Physicians, in particular, hath deservedly had the first reputation in their profession. Among the many eminent services which the authority of this learned and judicious body hath done to the practice of Physic it might not be the least that it had driven out this medley of discordant simples . . . made up of a dissonant crowd collected from many countries, mighty in appearance, but in reality, an ineffective multitude that only hinder one another'.

However, following Heberden's attack on the efficacy of the product in 1745 the 1746 *London Pharmacopoeia* was the last in which Mithridatum and Galene appear.

Table 1

Analysis of visitations by decade 1724–1754

Years	Number of visitations	Number of premises visited (average per visitation)
1724–1734	37	791 (21)
1734–1744	22	384 (17)
1744–1754	18	325 (18)
1756–1757	4	56 (14)

At this period the Julian Calender, with New Year's Day 25 March, was in use. From Visitation of Apothecary, Chymist and Druggist Shoppes, College of Physicians of London, in three volumes: Vol. 1 1724–1731; Vol. 2 1732–1747; Vol. 3 1748–1754. The final volume also contains records of four visitations for 14 April 1756, 21 June 1756 and 10 August 1756, at which William Heberden was one of the four Censors, and the last recorded visitation of 9 June 1757.

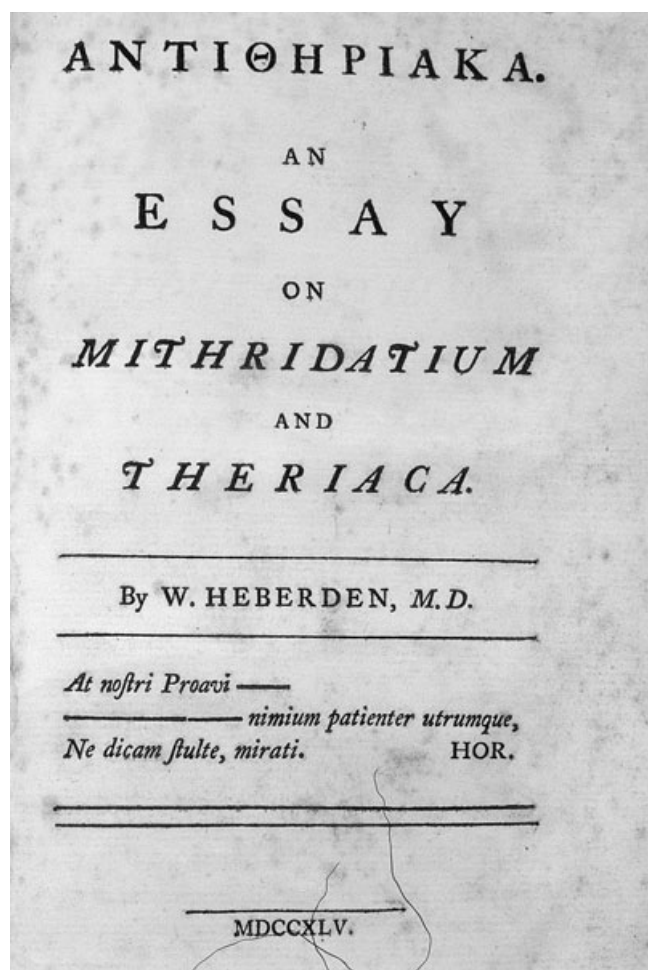


Figure 6

Title page of William Heberden's *Antitheriaca*, 1745

In the 1746 *London Pharmacopoeia* Theriac was listed with 61 ingredients and Mithridatium with 45 [30], virtually unchanged since Galen's recipe. The detailed directions for the preparation of Mithridatium were given in Pemberton's English translation of the 1746 *London Pharmacopoeia*.

Not all western European countries were so quick to expunge these formulations, for Galene with its vipers appears in the *German Pharmacopoeia* of 1872 and in the *French Pharmacopoeia* of 1884.

Conclusion

The two ancient products Mithridatium and Theriac Andromachus held central places in therapeutics for nearly two millenia. Concern for the quality of these products was the stimulus for requiring the public compounding of these preparations, later replaced by inspection of manufacture and examination of finished

Table 2

The development of concepts of medicines regulation in England as illustrated by the history of Mithridatium and theriacs

Regulatory measure	Date
Quality and inspection	1423, 1540, 1723
Fines for breach of Regulations	1540, 1553, 1617
Specified composition	1586
Licensing of specific manufacturer(s)	1586, 1625
Destruction of faulty product	1540, 1723
Pharmacopoeial monograph	1618, 1650, 1721, 1746, 1788
Fraud prevention	1688
Multidisciplinary scrutiny	1723
Appeal procedures	1723
Exemptions from legislation	1723
Efficacy	1745
Ideas of regulatory scrutiny prior to marketing	1799

product. These products were also the stimulus for the publication of pharmacopoeias in which standards for ingredients and the compounding of Mithridatium and Theriac Andromachus were laid down. Eventually these products were the first medicines to be challenged on grounds of efficacy. (Heberden also raised the problem of drug interaction from this polypharmacy.)

Perhaps in the final analysis, the contribution of Mithridatium and theriac to modern medicine was that concerns about their quality stimulated the earliest concepts of medicines regulation (see Table 2).

The *Medical and Physical Journal* [31], one of the earliest to supply regular information on new work in medicine, pharmacy, chemistry and natural history, suggested in its first volume in 1799: '... we would submit to the legislature the propriety of erecting a public board composed of the most eminent physicians for the examination, analysis and approbation of every medicine before an advertisement should be admitted into any newspaper or any other periodical publication and before it should be vended in any manner whatsoever'.

These views, stimulated not only by Mithridatium and theriac but also by the rise of patent medicines, were well ahead of their time and pre-empted the Medicine Act 1968 by 170 years. There is no doubt that the 1724 Act, because of its exemption of patent medicines from search by the College Censors, became known as the 'Quacks Charter'. The first use of the word 'Quack' in this context was in 1746 [32].

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