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Review Article

Experimental Screening Approaches for Evaluating *Muqawwi* and *Muharrik-i-A'sab* (Nervine Tonic and Stimulant) Drugs in Unani Medicine: A Translational Perspective

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Abstract

Objective (s): To establish a translational experimental framework for the scientific screening of Unani drugs described as *Muqawwi-i-A'sab* (nervine tonic) and *Muharrik-i-A'sab* (nervine stimulant) by identifying validated *in vivo* neuropharmacological models corresponding to the Unani concepts of nerve weakness and neuromuscular dysfunction.

Data Sources: Classical Unani literature and contemporary scientific publications were systematically reviewed. Electronic databases, including PubMed, Scopus, and Google Scholar, were searched to identify studies describing experimental neuropharmacological models relevant to nerve weakness, neuromuscular dysfunction, peripheral nerve injury, neuropathy, and neurodegeneration.

Study Selection: Validated *in vivo* models assessing muscle strength, motor coordination, neuromuscular function, peripheral nerve injury, and neuropathic disorders were included. Selected models comprised the grip strength test, rotarod test, wire hang test, sciatic nerve crush injury model, diabetic neuropathy models, chronic constriction injury, and spared nerve injury model.

Summary of the Contents of the Article: The reviewed models closely reflect the clinical manifestations of nerve weakness described in Unani medicine. Neuromuscular performance tests objectively assess muscle strength, endurance, balance, and motor coordination, while peripheral nerve injury and neuropathy models facilitate evaluation of neuroprotective, regenerative, and functional recovery effects. Together, these experimental drug screening approaches provide a scientifically robust framework for investigating the pharmacological activities of *Muqawwi-i-A'sab* and *Muharrik-i-A'sab* drugs and support their translational evaluation.

Conclusion: Validated experimental neuropharmacological models offer suitable translational tools for the scientific evaluation of *Muqawwi-i-A'sab* and *Muharrik-i-A'sab* drugs. Integrating these models with traditional Unani concepts can strengthen evidence-based validation of these medicines and advance pharmacological and translational research targeting neuromuscular disorders.

Keywords: Unani System of Medicine; *Muqawwi-i-A'sab;* Nervine tonic; *Muharrik-i-A'sab;* Nervine stimulant; Screening approaches.

Introduction

The term "neurological disorders" refers to conditions affecting the central and peripheral nervous systems,[1] including the brain, spinal cord, peripheral nerves, cranial nerves, nerve roots, neuromuscular junction, autonomic nervous system, and muscles.[2] The ancient Unani physicians were well aware of neurological disorders, Raban Tabri (780 AD- 850 AD) in his book, "Firdous-al-Hikmat" (Paradise of Wisdom) has described symptomatology and recommended therapies for organ specific diseases including neurological disorders like *Falij* (Paralysis), *Laqwa* (Facial palsy), *Ri'sha* (Tremor), *Kuzaz* (Tremor) and *Tashannuj* (Muscular spasm).[3] Abu Bakar Bin Zakariya Razi (Rhazes, 850-923 AD) in "Kitab-al-Mansoori" described the neurological disorders with their respective treatment,[4] and in "Kitab-al-Hawi, Vol. 01" (Liber Continent) explored the circumstances of neurological disorders and their treatment, which is purely based on the knowledge of his self-experience.[5] Ali Ibn Abbas Majoosi (Haly Abbas, 930 - 994 AD) in his book "Kamil-us-Sana" (Liber Regius) comprehensively describes *Aza-i-Nafsaniya* and their disorders (neurological disorder).[6] Hubal Baghdadi in his book, "Kitab Mukhtarat Fit Tib", explains the neurological disorders under the heading of *Amraz-i-Dimagh* and *Amraz-i-A'sab* and their management.[7] Allama Kabiruddin in his book, "Bayaz-i-Kabir" describes the

Usool-i-ilaj (Principles of treatment) of neurological disorders.[8] Ibn Rushd (Averroes, 1126-1198 AD) in his book, "Kitab-ul-Kulliyat" (Colliget), explained the *Ri'sha* and *Tashannuj* as the *Amraz-i-A'sab* (nervine disorder).[9]

Abu Ali Hussain Ibn Abdullah Ibn Sina (980–1037 AD), who is known as Avicenna in western countries, in his book "the Canon of Medicine," explained that the brain and spinal cord are the sources of nerves, and impairment of nerve functions can occur anywhere along their pathway." Ibn Sina divides the nervous disorder into two, one is *Amraz-i-Dimag* (brain disorders) and another is *Amraz-i-A'sab* (nervine disorders). He further stated and classified the *Amraz-i-Dimag* into four types. The first is *Suda'a* (headache); second, *Waram* (inflammation) and *Tafarruq-i-ittesal*, and under second type he described five disorders i.e. *Sarsam* (Meningitis), *'Utāsh*, *Waram Kharji* of head, *Ijtima*, *Aab-i-Sard*, *Subat Sahri* (coma vigil); under third disorders he has mentioned eight different diseases like *Subat* (Coma), *Sahar* (insomnia), *Nisyan wa Ikhtilat al-Dhihn* (amnesia and mental derangement), *Hizyan* (delirium), *Ru'unat wa Humq* (weakness of thinking faculty and idiocy), *Malankhuliya* (Melancholia), *Junun* (insanity), and *Ishq* (Erotomania); and under the fourth disorders he has described total seven diseases, *Sadr* (Giddiness), *Duwar* (vertigo), *Fayhadhaj* (Excessive lethargy and fatigue), *Kabus* (nightmare/incubus), *Sar'* (Epilepsy), *Sakta* (Unconsciousness), and *Jumud* (Catalepsy). [10]

He classified the *Amraz-i-A'sab* (nervine disoders), into ten types namely *Istirkhā'* (Flaccidity), *Fālij* (Paralysis), *Tashannuj* (Muscular spasm), *Tamaddud* (Stretching of muscles), *Kuzāz* (Tetany), *Laqwa* (Facial palsy), *Ri'sha* (Tremor), *Irtia'ād* (Momentary shaking of organs), *Khadar* (Numbness), *Ikhtilāj* (Fasciculation).[10,11] Ibn sina stated that *Hissi A'sab* (sensory neurons) are more sensitive than *Harki A'sab* (motor neurons) to accept pathological conditions, so chronicity of sensory neuropathies may lead to motor dysfunctions. [10,12] *Falij* is a disease of nervine disorder causing loss of sensory and motor function in the longitudinal half of the body sparing the face and this occurred because of the stoppage of *Ruh-e-Hassas* (sensory pneuma) and *Ruh-e-Muharrik* (motor pneuma) into the organs. Another cause is that the *Ruh* may reaches to the organs but the organs not able to accept the *Ruh* due to *Fasad* in their *Mizaj*. [10,13,14] Abnormal *balgham* or excess *burudat* and *rutubat* lead to *murkhi* (pseudohypertrophy) and abnormal *hadm udwi* leads to *Istirkha* (Flaccidity). *Istirkha* is one of the important nervine disorders in which the movement of the organs is completely stopped or reduced.[15] Another nervine disorder which is related with nervine weakness is *Ra'sha,* Shivering of the organs of the body due to the weakness or defect in motor system. Same as *Khudr* which develops due to the weakness or defect in sensory system. Loss of sensory faculty in nerves and muscles is known as *Khudr.*[11] *Irq al-Nisa* (Sciatica) is an Arabic word that represents the "name of a nerve" which starts from gluteal region and followed up to the ankle, because the pain is associated with this (sciatic nerve) that's why it is termed as *Irq al-Nisa.* Many Unani scholars like *Ibn Sina, Ismail Jurjani, Zakariya Razi, Ibn Zuhar* also describes the *Irq al-Nisa* in the same way. [11,16]

The treatment of nerve disorders are very well explained in Unani literature and great ancient Unani physicians have treated these disorders by *Muqawwi* and *Muharrik-i-A'sab* drugs. The *Muqawwi-i-A'sab* drugs are describes as the drugs that tone up the nerves and prevent the absorption of morbid matter. These drugs restore the normal functions of the nerves and increase their vitality.[17] The *Muharrik-i-A'sab* drugs act on nerves show more prominent effect on nerve endings of sensory and motor, than axons, and stimulate them therefore used in muscle weakness.[18]

From the above literature it is clear that the diseases of CNS can lead to severe motor impairment in gait and fine motor skills. [19] And evaluation of muscle strength is a crucial first step to study neuromuscular disorders in rodent models. In contemporary medicine a number of invasive and non-invasive techniques have been developed to measure the muscle strength of rodents. The invasive muscle force measuring techniques, which include *in situ* and *in vitro* measurements, whereas non-invasive techniques include *in vivo* measurement of muscle force, wire hang tests, rota rod, photoactometer, grip strength tests, treadmill testing, and, vertical pole tests, and etc. [20]

Since ancient times several *Muqawwi* and *Muharrik-i-A'sab* (nervine tonic and stimulant) drugs in Unani Medicine are being used in the management of nervine disorders, despite their extensive therapeutic use in Unani practice, there are lack of well-defined experimental screening methods to scientifically evaluate their pharmacological actions. Therefore, the present study was conducted to develop a translational experimental framework for screening *Muqawwi* and *Muharrik-i-A'sab* drugs using symptom-based *in-vivo* models of nerve weakness and neuromuscular dysfunction.

Methodology:

The present study entitled "Experimental Screening Approaches for *Muqawwi* and *Muharrik-i-A'sab* (Nervine Tonic and Stimulant) Drugs in Unani Medicine: A Translational Perspective" was undertaken in the Department of Ilmul Advia, National Institute of Unani Medicine (NIUM), Bengaluru.

Source of Data

The present study data was collected by a comprehensive survey of Unani classical and conventional literature. A narrative review of the published literature was also conducted to identify experimental neuropharmacological models relevant to nerve weakness and neuromuscular dysfunction.

Method of Collection of Data

1. Literature survey

A manual survey of almost all the classical Unani books published in different languages (Arabic, Persian, and Urdu) was conducted to collect the information available on the concept of nervous disorder, *Muqawwi* and

Muharrik-i-A'sab drugs. Then symptom-based screening methods were collected from contemporary books and different research papers based on neurological disorders including nerve weakness and muscle weakness. A comprehensive search of electronic databases like PubMed, Science Direct, Research Gate and Google scholar was referred to gather all the information.

2. Inclusion and Exclusion Criteria

Those research studies in which experimental models were used for assessing neuromuscular function or nerve injury were included.

The studies which did not describe experimental screening methods related to nerve function and were unrelated to neuromuscular or neuropathy models and duplicate or incomplete reports were excluded.

Experimental Screening Methods for Evaluation of *Muqawwi* and *Muharrik-i-A'sab* Drugs

1. Dynamometer

A dynamometer is used to measure rodent (mouse) forelimb muscle strength and the duration of pull (endurance). A mouse suspended by its tail, this instrument measures the mouse's tendency to grip a horizontal metal bar. By first enabling the mouse to grab the bar and then exerting a downward force that gradually increases on the opposite end of a cable that the mouse is attached to, a threshold value for the amount and duration of force that the mouse can exert is determined. To provide a permanent record of the force generated by the mouse, the bar is connected to a force transducer and pen recorder. [20] (Fig. 1)

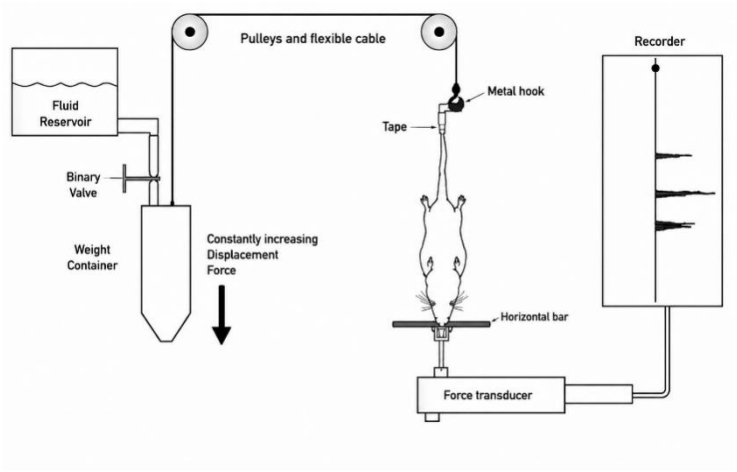

Fig.1: Mechanical diagram of dynamometer

2. Kondziela's inverted screen test

The inverted screen test is discovered by Kondziela in 1964. The inverted screen is a made up of 43 cm square of wire mesh consisting of 12 mm squares of 1 mm diameter wire. To prevent escaping of animal by climbing on the other side it is surrounded by a 4 cm deep wooden beading. (Fig. 2)

Procedure:

First place the small rodent (mouse/rat) in the center of the wire mesh screen, start a stop clock, after 2 seconds rotate the screen to an inverted position, with the animal's head declining first. Hold the mesh screen 40-50 cm above a padded surface. Stop the stop clock and note the time when the mouse falls off, or remove it when the criterion time of 60 sec is reached, a cut off time.

Scorings of the inverted screen: [21, 22.23]

Falling 1-10 sec = 1
Falling 11-25 sec = 2
Falling 26-60 sec = 3
Falling after 60 sec = 4

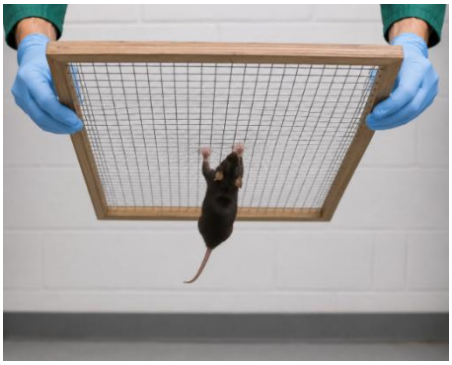

Fig. 2: Kondziela's inverted screen test

3. Weights test

The weight test is used to assess four limb strength in animals. The apparatus consists of seven weights. Each weight consists of a ball, tangled fine gauge stainless steel wire, weighing 7 gram and a series of steel chain links. The number of links ranges one to seven weighing 20, 33, 46, 59, 72, 85 and 98 grams. [21] (Fig. 3)

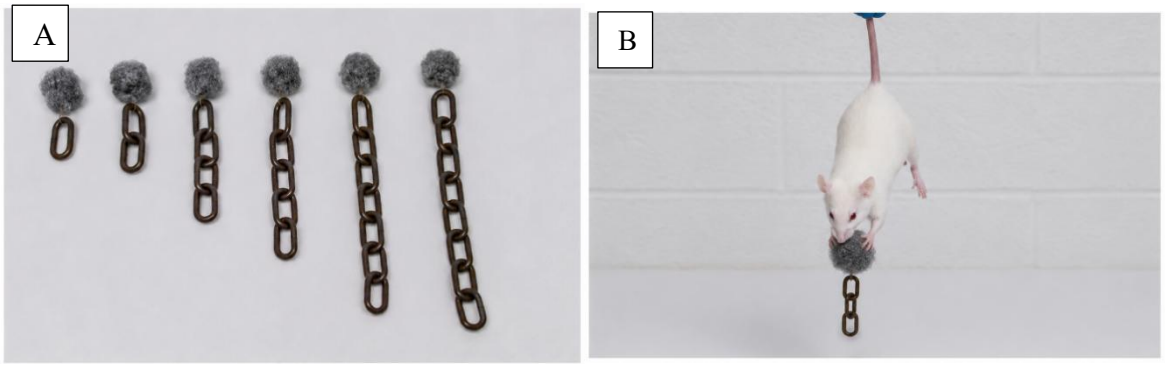

Fig. 3: (A) Weights, ranging from 20 g to 98 g, (B) A mouse weightlifting

4. Wire hang test or Hanging wire test

This test is used to assess forelimb strength in rat [24] and mice [25].

The test is based on the latency of an animal to fall off from a metal wire upon exhaustion. The apparatus consists of different length and diameter for mice and rat. To measure the rat grip strength, a stainless-steel wire (90 cm length, 3 mm in diameter), fixed horizontally between two vertical supports to avoid vibration or unwanted displacement and 60 cm above a soft padded surface. The rat is allowed to grasp the central position of the wire with its forepaws. The latency (s) to fall from the wire to the flat soft pad is measured. [24] (Fig. 4)

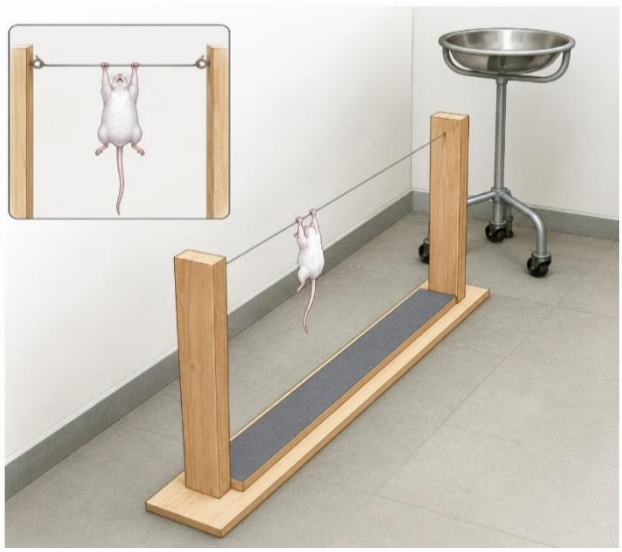

Fig. 4: Wire hang test Apparatus

5. Grip strength meter

A grip strength meter is used to assess muscle strength [26] in rodents. After training, to establish reliable assessment of gripping ability grip strength test has to be performed. Animal is positioned by facing the T bar of the grip strength meter and the forelimbs of rat are placed on the tension bar. When the rat grasped the bar, the animal is gently pulled steadily by the root of the tail away from the T bar. The grip strength meter determined and recorded automatically the maximum force displayed by each animal in grams. Rat has to be allowed to recover for 30 s between the measurements.[27,28] (Fig. 5)

Fig. 5: Grip strength meter for muscle strength assessment

6. Rota rod test

The rota rod test was first discovered by Dunham and Miya in 1957.[29,30] The Rota rod test is widely used to evaluate the locomotor coordination [31] and balance in rodents.[24] Rota rod apparatus is available with different accelerating rod diameter size for mice [30] and rat. To achieve the stability animals are pre-trained for the trail day, then place the rats on accelerating rota rod (IITC rota rod, 5, 10, 15, 20 and 25rpm) four times for five minutes in each trial. After the treatment, animal is placed on rod with gradually increase revolution per minute (rpm) for 5 minutes, taken as cut off time. Rest time between the consecutive trials should be given to animals. The time in seconds, distance in meters and rpm are automatically registered.[23,24,32,33,21] (Fig. 6)

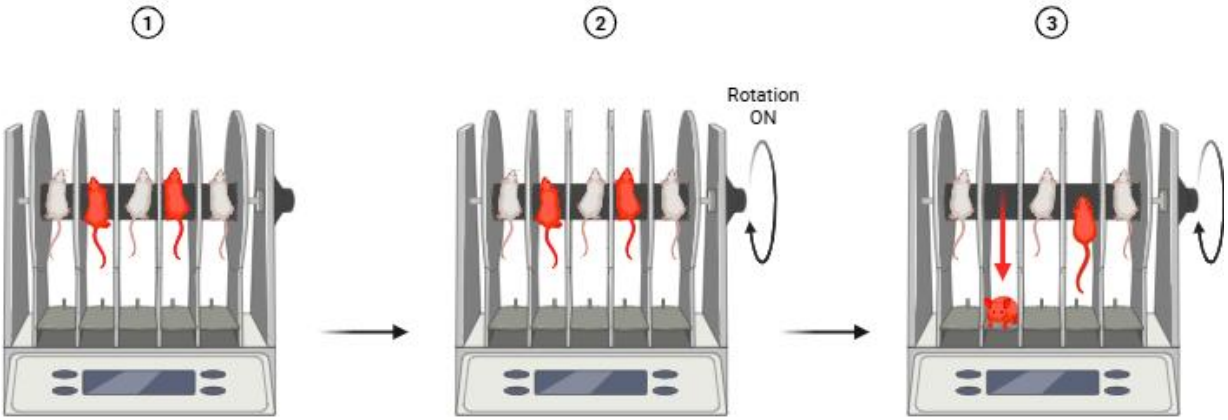

Fig. 6: Rotarod Mice/Rat balance on a rotating rod, and their latency to fall is recorded as the endpoint measure.

7. Photoactometer

The locomotor activity can be easily studied by using photoactometer.[34] The locomotor activity can be measured by using a photoactometer which operate on photoelectric cells which are connected in circuit with counter. When the beam of light falls on a photocell is cut off by the animal, a count is recorded. A photoactometer have arena in which the animal moves. This equipment is used for both rats and mice. [34] (Fig. 7)

Fig. 7: Photoactometer

8. Muscle torque

Muscle torque measurement is a commonly used *in vivo* method for assessing skeletal muscle strength without disturbing the anatomical integrity of the muscle. In this method, the limb is stabilized using a trans-osseous needle, while the foot or distal limb is attached to a footplate connected to a torque sensor and stepper motor. The corresponding motor nerve is stimulated through subcutaneous electrodes to evoke muscle contraction. Optimal stimulation parameters, including joint angle, voltage, and pulse frequency, are determined before recording maximal isometric torque. The generated torque during twitch and tetanic contractions is then recorded and analysed to evaluate muscle contractile function. This method also allows repeated measurements in the same animal over time and can be used for inducing eccentric contraction–mediated muscle injury.[35] (Fig. 8)

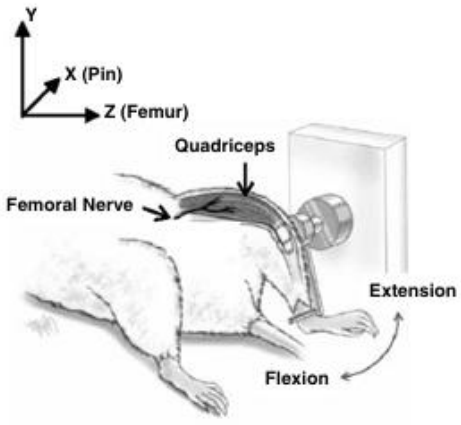

Fig. 8: *In vivo* torque apparatus

9. Muscle tension

Muscle tension measurement is an in vivo method used to determine the contractile force of an individual muscle. In this technique, the distal tendon of the target muscle is surgically exposed, severed, and attached to a load cell using a non-absorbable suture. The limb is stabilized, and the corresponding motor nerve is stimulated using subcutaneous electrodes. The load cell mounted on a micromanipulator enables adjustment of the muscle to its optimal resting length for maximal force generation. Muscle tension is recorded during single twitch and tetanic contractions after optimizing stimulation voltage and pulse frequency. This method provides direct measurement of muscle force and allows assessment of parameters such as maximal contractile tension and muscle fatigue.[35] (Fig. 9)

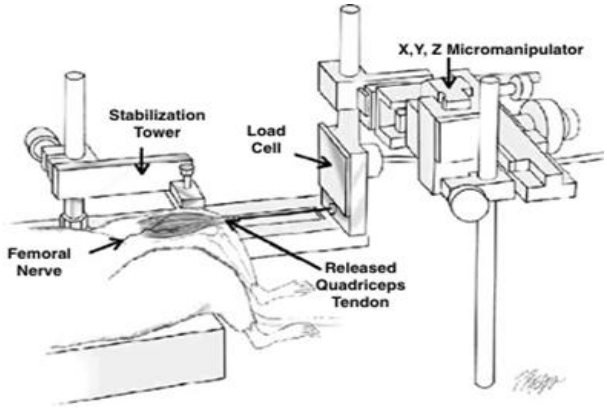

Fig. 9: *In vivo* tension apparatus

10.Triple-horizontal bar

A Triple-horizontal bar is used to measure coordination and forelimb strength. The bars are made of brass, 38 cm long, held 49 cm above the bench surface by a wooden support column at each end. The columns are secured to a heavy wooden base. Three bar diameters are available: 2, 4 and 6 mm. The 2 mm bar is the standard one, but many mice reach maximum scores on this. Therefore, larger diameter bars are preferred in an attempt to refine the test, as mice cannot grip these so well. (Fig. 10)

Scoring the horizontal bars[21, 36]

Falling between 1-5 sec = 1
Falling between 6-10 sec = 2
Falling between 11-20 sec = 3
Falling between 21-30 sec = 4
Falling after 30 sec = 5

Placing one forepaw on a bar support without falling = 5

Fig. 10: Triple-horizontal bar apparatus

11.Static rod

The Static rod is used to measure the muscle coordination in rodents. The static rod takes two measures: the orientation time and transit time. Five wooden dowels or rods of varying thickness 35, 28, 22, 15 and 9 mm diameter respectively; and each 60 cm long, are fixed by a G-clamp to a laboratory shelf such that the rods horizontally protrude into space. The end of the rod near the bench has a mark 10 cm from the end, to denote the finishing line. The height of the rods above the floor is 60 cm. For a shorter and less detailed test use only the largest, smallest and middle rods. [21] (Fig. 11)

Fig. 11: Static rod apparatus

12.Parallel bar test

This test is appropriate for the study of motor coordination in mice. The apparatus is composed of two metal bars, each 1 meter (1 m) long and 4 mm in diameter, and placed on a wooden platform which is raised 60 cm above by a wooden support. The metal bars are kept equidistant from each other (30 mm apart) along the entire length of the apparatus, and a stopwatch is used to record the time (in seconds) spent for each animal to turn a 90° on the double bar, and the time spent by each mouse to travel to one end of the bars. [21,36] (Fig. 12)

Fig. 12: Parallel bar apparatus

13.Treadmill Test:

Treadmill test is used to evaluate exercise capacity and endurance in rodents. Treadmill is inclined in two different angles; one in uphill inclination and another is downhill inclination. The uphill inclination caused uphill running which involves concentric contraction of muscle. Downhill running involves eccentric muscle contraction. Mostly uphill running is used. [37] The mice are placed on a treadmill with an uphill inclination of 30°, the treadmill is set for 5 minutes at the speed of 5 m/min followed by accelerations in speed up to 17 m/min. The test is stopped when the mouse remains on the shocker plate for 20 s at this point the time of exhaustion is determined.[38] (Fig. 13)

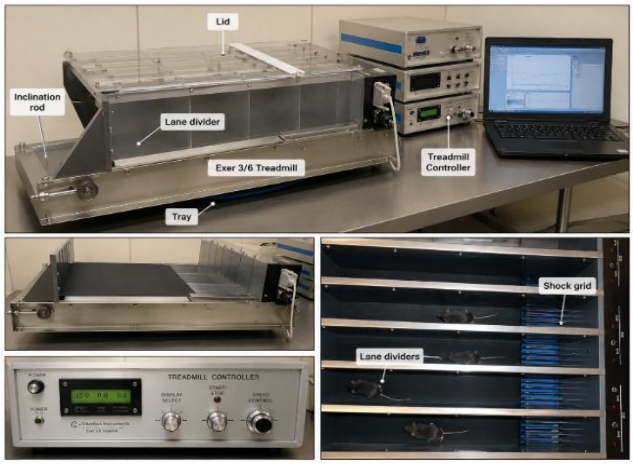

Fig. 13: Treadmill system and components

14. The study by Meffert et al. (2008) used a non-invasive transcutaneous electrical nerve stimulation (TENS)-based isometric muscle force measurement method for the assessment of muscle strength in rabbits. In this method, the force generated during dorsiflexion of the foot was measured by electrically stimulating the peroneal nerve through surface bipolar electrodes placed near the fibular head. The animals were positioned in a specially designed "beach chair" that maintained the hip, knee, and ankle joints at 90° to ensure isometric contraction of the tibialis anterior muscle. A strain gauge–based force transducer connected to a PowerLab recording system was used to record the force produced during muscle contraction in real time. This setup allowed quantitative, reproducible, and non-invasive evaluation of muscle strength and recovery following musculoskeletal trauma. [39] (Fig. 14)

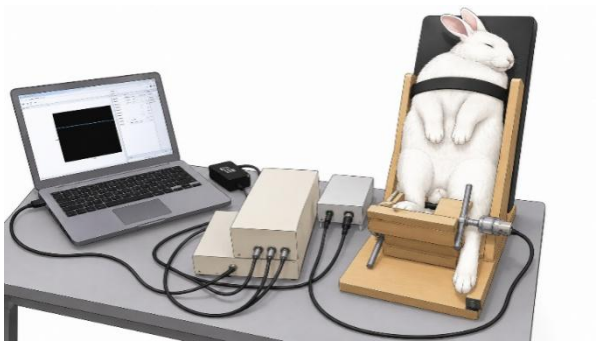

Fig. 14: The measuring unit consisted of a PowerLab unit, amplifier, bipolar electrode, force transducer, and a specially designed "beach chair." The force output generated during each contraction will be monitor and record in real time on the computer screen.

15.Strength-testing equipment

This equipment has been designed and constructed by Engineering Services at Dstl (Defence Science and Technology Laboratory), Porton Down, Wiltshire, England**.** It is designed to measure the muscle function in marmosets (tiny monkey). The majority of the testing device has constructed from clear Perspex and can be attached to the front of the cage. The arrangement of the key components of the system, includes a T-bar facing the marmoset which has been connected to variable weights via a pulley system. Displacement of this T-bar opens a simple gravity-fed dispenser containing a food reward which then drops to a retrieval chamber below.

Procedure:

1. Familiarize the animal with the reward.
2. Familiarize the animal with the strength-testing instrument, considered it as training.
3. Retrieve reward from kit by placing the reward into reward retrieve chamber.
4. Tap and slide back and forth of T-bar to attract the attention of animal.
5. Now add the weight, start with 10g, to receptacle. If marmoset pulls the weight successfully three times, add extra weight. For each session limit the weight increment up to five. If animal not able to displace the weight, then repeat the previous stage.[40]

16.Open Field Test

The Open field test used to measure general locomotor activity in rodents.[23,24,41] The first open field study for rodents was conducted in 1934 by Hall (1934) for emotionality in rats.[42] The open field apparatus is

constructed of white plywood and measured 72 × 72 cm with 36 cm walls. One of the walls is covered with a Plexiglas so the rats could be visible in the apparatus. Black lines are drawn from the floor with a marker and are visible through the glass. A central square is drawn in the middle of the open field. Each rat is placed in the centre of the square and observed for 5 min. Line crossing, stretched-attend posture, rearing, grooming, centre square and freezing duration are recorded.[41] (Fig. 15)

Fig. 15: Open Field Test Apparatus

17.Catwalk

Catwalk apparatus is used to measure the motor coordination in rats.[21]

In this apparatus Gait analysis is performed by using the Catwalk XT system (Noldus, Leesburg, VA, USA).

Procedure:

1. Allow the animals to walk freely across the runway made up of glass to reach goal box consist of an empty cage with animal bedding.
2. In the test a mouse moving across the runway without stopping or changing directions within a time frame of 0.5 to 5 s is considered as compliant run. Three compliant runs made up the testing trial.
3. To captured the silhouette of the animals the ceiling of the runway illuminated by red light.
4. A green light enters at the edge of the glass runway and is internally reflected; light escapes each time a paw makes contact with the glass.
5. A digital high-speed video camera positioned under the Catwalk for Paw prints and silhouettes.
6. Catwalk XT 8.1 software (Noldus) is used to analyse the data.[43,44]

Scales to measure the locomotion

18.Basso, Beattie and Bresnahan (BBB) and Basso Mouse Scale (BMS) locomotion rating

The Basso, Beattie and Bresnahan' (BBB) developed a scale for rats and the 'Basso mouse scale' (BMS) for mice to evaluate locomotion after spinal cord injury (SCI) which is based on observer ratings while the animals move around in an open field. [45] The BBB scale is 21point rating scale, while BMS consist zero to nine points.

Procedure:

a. Open field habituation is required before starting the trial.
b. After habituation animals are allowed to move freely for four minutes and individual limb behaviour is scored directly by at least two blinded observers or it can be filmed for offline analysis.[44]

Assigned score in the BMS

No ankle movement = Zero (0)

Single ankle movement = 1

Extensive ankle movement = 2

Plantar placing of the paw with or without weight support = 3

Occasional plantar stepping = 4

Frequent or consistent plantar stepping, no coordination = 5

Frequent or consistent plantar stepping, some coordination, paws parallel at initial contact = 6

Frequent or consistent plantar stepping, mostly coordinated, paws parallel at initial contact and rotated at lift off = 7

Frequent or consistent plantar stepping, mostly coordinated, paws parallel at initial contact and lift off, and mild trunk instability = 8

Frequent or consistent plantar stepping, mostly coordinated, paws parallel at initial contact and lift off, and normal trunk stability and tail always up = 9 [45]

19.Bederson Scale

Bederson scale is used to measure neurological impairment;[46] for example, in stroke it is used to measure paw asymmetry and balance. [44] Tests include resistance to lateral push, forelimb flexion, and circling behaviour. [46]

20. Garcia scale

Garcia scale is used to measure the paw asymmetry, general mobility, grip strength, reaction to sensory stimuli. [44]

21. Modified neurological severity score (mNSS)

Modified neurological severity score is used to measure Paw asymmetry and balance, general mobility and reaction to sensory stimuli. It consists of six tests with 0-6 point each.[47]

22. Neurologic Deficit Scale

The 24-point neurological deficit scale is often used in the motor function tests. It is the most convenient assessment and doesn't require any apparatus. For mice, the researcher should observe 6 aspects, including body symmetry, gait, climbing, circling behaviour, front limb symmetry, and compulsory circling.[47]

Test to measure fine motor skills

Fine motor skills, such as closing a zipper or picking up a pen, are vital in daily life of humans. [44] But these fine motor skills can be abolished by a number of movement

disorders, neurological disorders include stroke, spinal cord injury, traumatic injury[48] and neurodegenerative disorders like Parkinson's disease and Huntington's disease.[49] Given that animals cannot accomplish the same activities, it initially seems difficult to recreate these abilities in animal models. Nevertheless, rodents have a strong grasp and excellent mobility. A challenging testing environment is required because rodents' fine motor skills aren't always visible in their home cage. [44]

23.Single pellet reaching test

The "single pellet reaching test," also known as the "skilled reaching test," created to give an understanding of grasping activity in rats. [44] The rat is taught to reach outside of a reaching box, through a tiny opening on a shelf, and take up a single food pellet with its favoured paw. The rat is taught to walk to the back of the box after each reach, turn around, and walk back to the slot to start the next trial. This procedure is crucial because it compels the rat to realign and reposition its body inside the reaching box rather than turning around and twisting around its own axis in front of the slot. A total of 20 food pellets are consumed throughout training sessions on each experimental day. A successful reach is one in which the food pellet is successfully reached for, grasped, and consumed. First trial success or overall success is two ways to describe successful reaches. Finally, the total number of attempts can be given as an indicator for every forelimb motion made in the direction of the food pellet. Scores are calculated for the first three successful reaches, and the results are shown as either a total score or the average score for each movement component. [44,49,48] (Fig. 16)

Fig. 16: Single pellet reaching test

24. Staircase test

The staircase test also called the "paw-reaching test" originally introduced by Montoya and collaborators to evaluate a rat's ability to pick and reach small objects by using its forelimbs.[50] In this test a Plexiglas enclosure installed on a pedestal contains the animals. The animals have to reach through a slit in the front wall to access food pellets that are on a shelf outside through a passageway made of two Plexiglas walls inside that box. The food pellets are strategically positioned in tiny divots on the left and right side of the shelf to stimulate reaching with the opposing forelimb. Pellet reaching is captured from the front, bottom, and/or side to frame-by-frame measure forelimb motion.[44] (Fig. 17)

Fig. 17: The staircase test

25. Adhesive removal test

The adhesive removal test is used to measure the sensorimotor neurologic deficits of both forepaws of rodents. The equipment needed the adhesive tape and a scissor. Cut the tape by using the scissor into small circular or square pieces, the diameter or length is around 6mm for rats and 4mm for mice. Gently attach the tape on fore paws with equal pressure. The latency of removing the tape is taken from the time the animal notices the tape until the tape is removed by the animal. The cut off time taken as 120-180 seconds. Three-day pre-training is required to adopt the condition of put on the tape and removing the tape within 10 seconds. [44,47] (Fig. 18)

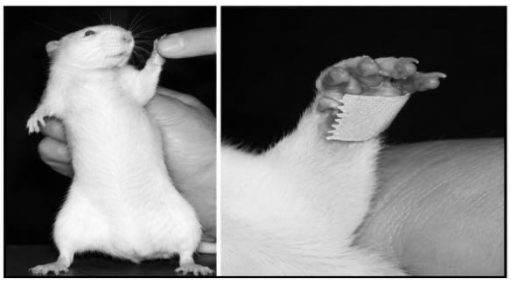

Fig. 18: Adhesive removal test

26. Grid Walk Test (GWT)

The grid walk test (GWT) is used to measure the sensory-motor coordination.[47] The apparatus consists of an overhead grid; opening of grid is 2-3 cm for rat, which connects two tall walls. For the trial put the animal on grid and allow walking for three minutes. Sleeping of foot fault and total number of steps are recorded.[44,47] (Fig. 19)

Fig. 19: Grid Walk Test (GWT)

Discussion

According to Unani literature that *Muqawwi* and *Muharrik-i-A'sab* drugs are used to manage neurological disorders, as *Muqawwi-i-A'sab* drugs strengthen the nerves and *Muharrik-i-A'sab* drugs act on nerve terminals and improve the motor functions. To evaluate the pharmacological actions of *Muqawwi* and *Muharrik-i-A'sab* drugs there are no suitable screening methods available. Therefore, in the present study, suitable screening methods for these drugs have been explored. The selection of screening methods was done by considering the symptoms of neurological disorders, comprising both central and peripheral disorders. These disorders include 1. Neurodegenerative disorders: like Parkinson's disease, Alzhiemer's disease; cerebrovascular diseases, like stroke. 2. Neuromuscular disorders: like peripheral neuropathy, muscular dystrophies, and myasthenia gravis which directly or indirectly leads to loss of motor functions of the body. There is a battery of screening models available in Contemporary research which are used to check the muscle strength, muscle coordination, muscle force, fine motor skills in animals like wire hang test,[24] photoactometer,[34] rota rod,[21,23,24] dyanometer,[20] kondziela's inverted screen test,[21] weight test,[21] grip strength test,[27,28] horizontal bar test,[21] static rod,[21] treadmill test,[38] catwalk,[43,44] BBB,[45] BMS,[46] Bederson,[44] Garcia,[44] mNSS,[47] neurological deficit scale,[47] single pellet reaching test,[44] stair case test,[44] adhesive remove test and Grid walk test.[44,47]

By correlating these modern experimental approaches with the classical Unani concepts of nerve weakness, it becomes possible to develop a scientific framework for evaluating the pharmacological activity of the drugs categorized under *Muqawwi* and *Muharrik-i-A'sab*. Such an integrative approach may help bridge the gap between traditional knowledge and modern biomedical research, thereby contributing to the scientific validation of neuroactive drugs used in Unani medicine.

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50. CHAPTER B7 - Utility of 6-Hydroxydopamine Lesioned Rats in the Preclinical Screening of Novel Treatments for Parkinson Disease Author links open overlay panel M. ANGELA CENCI, MARTIN LUNDBLAD