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Full Length Research Paper

An improved technique for oral administration of solutions of test substances to experimental rats using Mediflon/Medicut intravenous cannula

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The oral administration of solution of drugs or test substances to experimental rats is often necessary in various pharmacological, toxicological and other biomedical researches. It is scientifically sound and preferable to administer test substances to experimental animals by the same route(s) by which it is taken or meant to be taken by humans as systemic bioavailability; pharmacokinetics and toxicological parameters obtained for the substance will depend markedly on the route used to administer it. The non-ready availability of the standard oral cannula designed for varieties of animals and widespread dearth of technical skills to properly use available improvised techniques in this part of the world has made this route somewhat unpopular among biomedical scientists. In several instances it is abandoned even though initially opted for. This paper narrates and illustrates the technique of using a size 18G Mediflon/Medicut intravenous cannula as an improvised oral cannula to administer solutions of drugs and test substances to experimental rats. Techniques of handling and manipulating the rat with the goal of having the eosophagus as straight as possible and of the oral introduction of the Mediflon/Medicut cannula attached to a syringe containing the solution of test substance are narrated and then illustrated by pictures. The usual problems and difficulties encountered with the oral administration of solutions of test substances using either the syringe alone or introducing it into the feeds or drinking water of the rats were avoided. And the intended doses were accurately delivered at every instance this improvised oral cannula was used.

Key words: Oral administration, Mediflon/Medicut intravenous cannula.

INTRODUCTION

Oral ingestion is the most common method of drug administration to humans. It is also the safest, most convenient and most economical route (Barar, 2000). Parenteral therapy is indicated when it is impossible to use the oral route as when the individual is uncooperative unconscious or unable to retain anything given by the mouth.

Oral administration of test substances or drugs in solutions to laboratory rats is ideally done with the aid of specially designed size 18G steel or plastic cannulas that are not readily available in this part of the world (Abioye et al., 2003).

As a result the performance of this task by several researchers working with rats is made a difficult one. This paper describes the use of the readily available intravenous cannula as an improvised oral cannula for the administration of solutions of test substances to laboratory rats.

MATERIALS AND METHODS

Materials

Mediflon/Medicut intravenous cannula (18 x 1.3 x 45 cm) with injection valve (Eastern Medikit Ltd), syringes (1, 2, 5 and 10 ml),

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Figure 1. Materials required: Mediflon/Medicut intravenous cannula, plastic syringes (1, 2, 5 and 10 ml).

Figure 2. Aspirating the extract from the flask with a 10 ml syringe.

solution of drug or test substances, beaker and towel.

Animal handling

The oral administrations of drugs to laboratory rats require extensive handling and it is recommended that prior to experimental manipulation, such animals should be handled on a regular basis in non life threatening situations like weighing, petting, giving food treats. This makes the animals respond positively to handling and learn to recognize individuals. The animals should be handled gently but firmly avoiding loud noises or sudden movements (Risdahl, 2006).

To remove the rat from the cage, it is picked up by the tail close to the base and placed on the flat surface of a laboratory bench. While still holding to the tail with the right thumb and forefinger, the scruff of the animal is reached for with your left thumb and forefinger, positioning them firmly on either side of the animal's head at the level of the mandible. Simultaneously the rest finger and palm of the left hand are used to firmly press the thorax or trunk down against the flat surface of the bench. Thereafter the scruff (the loose skin over the neck) is gathered between the thumb and the forefinger and used to lift up the animal by the scruff. The tail may be held either firmly against the trunk with the fifth finger of the left hand or left hanging free. When held firmly this way, the rat is restrained and the esophagus is as straight as possible. For an aggressive animal not well acclimated to handling and with the absence of a bite proof hand glove, the above technique can still be used with a towel sandwiched between the left hand and the animal body all the way (Figures 1 to 10).

Figure 3. Connect the Mediflon intravenous cannula to the 10 ml syringe containing the test solution.

Figure 4. Rats in the cage.

Administration of the test substance/drug

The cannula is inserted into a desired syringe containing the solution of drug or fluid test substance and held with the right (dominant) hand. It is introduced into the animal's oral cavity with the plastic tube tilted to the left side of the animal's incisor teeth in the midline and maintained in this position throughout the procedure to avoid damage to it from the animal's bite. The tube is now carefully advanced down the oral cavity between the tongue and roof of the mouth, occasionally it passes easily straight on into the esophagus at other times a resistance is encountered. This resistance can be relieved by the maintenance of a gentle inward push on the cannula while rotating the tip from side to side. This soon stimulates a swallow reflex, which transmits the cannula into the esophagus. Occasionally the animal may use any of its strong hands to attempt to push the cannula out of the mouth at this stage or during the injection. Working alone in this situation, instead of focusing on restraining the tail as explained above it greatly helps to use any of the other free fingers of your left hand to hold down the

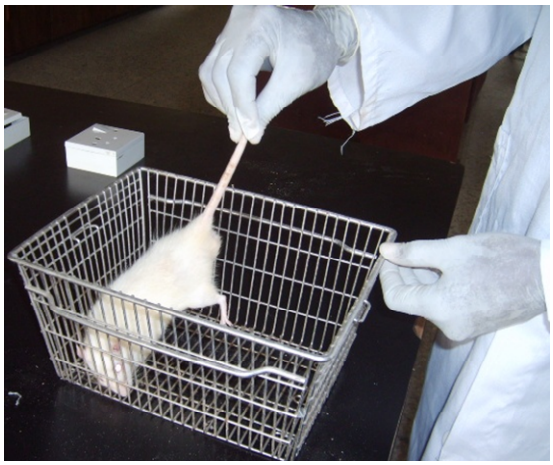

Figure 5. Picking the Rat by the tail to remove it from the cage.

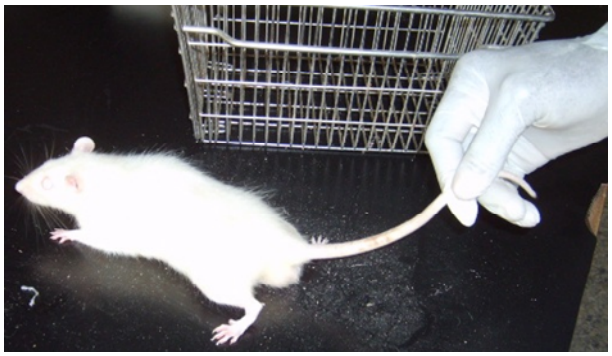

Figure 6. Rat placed on the flat surface of the laboratory bench.

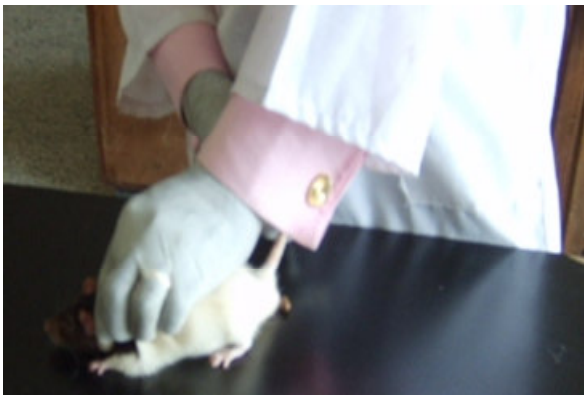

Figure 7. Restraining the rat against the flat surface of the Laboratory bench.

dominant forelimb of the animal preventing any grip on the cannula already situated within the esophagus. Once in the esophagus the plunger is pushed down the syringe, emptying its content into the esophagus en-route to the stomach (Figures 11 to 13).

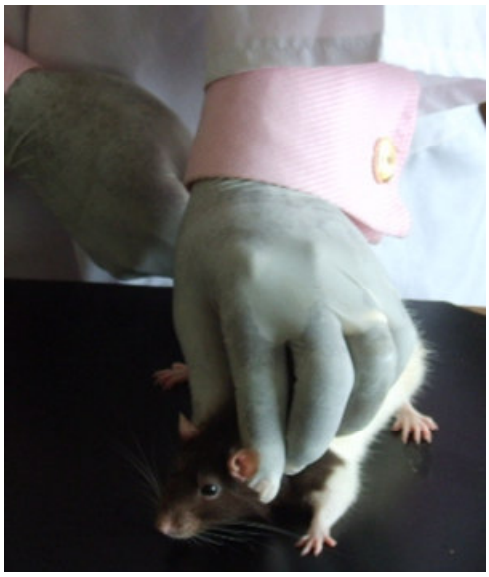

Figure 8. Gathering the scruff (loose skin over the neck) with the index finger and thumb by the mandible.

Figure 9. Rat picked up by the scruff and held with the eosophagus kept as straight as possible.

RESULTS AND DISCUSSION

The oral administration of solution of drugs or test substances to experimental rats is often necessary in various pharmacological, toxicological and other biomedical researches. Although the parenteral routes like subcutaneous, intra-peritoneal and intramuscular routes provide ready alternatives to the oral route, it is scientifically sound and preferable to administer the test substance to experimental animals by the same route(s) by which it is taken or meant to be taken by humans. This is because systemic bioavailability, pharmacokinetics and toxicological parameters obtained for the substance de-

Figure 10. Restraining the rat by the scruff with a towel sandwiched between the hand and animal.

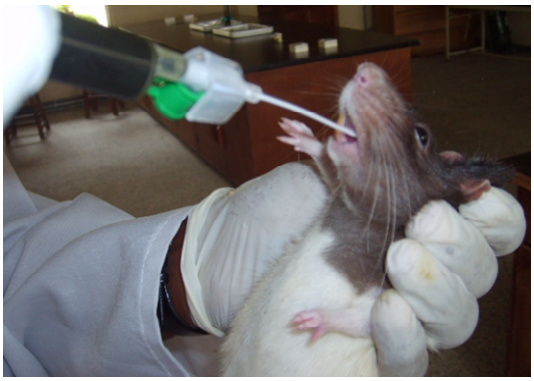

Figure 11. Inserting cannula tip by the left side of the rat's central canine. Rotating the tip in the oropharynx to overcome resistance.

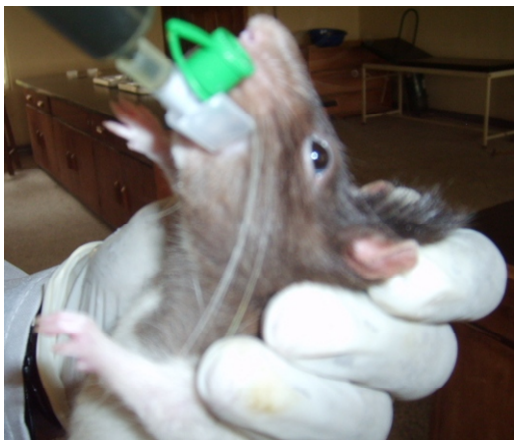

Figure 12. Entire length of cannula tube inserted with tip well lodged in the oesophagus.

pend largely on the route used to administer it (Wilkison, 2001).

The none ready availability of the standard oral cannula designed for the varieties of laboratory animals and a

Figure 13. Injecting the test solution into the oesophagus of the rat by pushing down the plunger of the syringe.

widespread dearth of technical skills in properly using available improvised techniques in this part of the world has made the oral route somewhat unpopular amongst biomedical scientists working with rats.

It is not uncommon for the oral route even though initially preferred and ideal for the administration of the test substance to the laboratory rats to have been abandoned by researchers because of the difficulties encountered in the process.

There have been a number of different improvisations resorted to by researchers to circumvent this problem. The use of 5, 2 or 1 ml syringes to measure a volume of a stock solution that convey the required dose of the test substance and then administering it orally by pushing the plunger downward is not an uncommon practice among biomedical researchers in this part of the world. Many of these are probably reported in research methodology, merely stating that the experimental animals were fed orally without any accompanying details of how the animals were actually fed the solution of drugs or test substances (Obasi and Njoku, 2000; Oladiji et al., 2005). This technique you would agree may be highly error prone in terms of the actual amount of the solution of drugs or test substances the animal eventually ingests. This is largely due to the high occurrence of loss of the test substance as a result of spillage due to either over-flow or regurgitation by the animal. This annoying experience is often narrated or excused by the researcher as the animal refusing to take the test substance orally.

Many insincere researchers have gone ahead to report

their intended doses of the test substances to have been administered even in the face of this setback choosing to ignore the fact that such extraneous losses of the test substance could certainly affect the validity of any conclusions made from such studies, especially where the test substance unknown to them possesses a narrow therapeutic index. Another commonly encountered problem when this technique is used is that there is high probability of the test substance getting aspirated into the lungs resulting in aspiration pneumonitis that can cause the death of the animal within 24 to 72 h of an administered dose. This has led to the adoption of erroneous total lethal oral dose (LD_{100}) and wrong computation of the median lethal doses (LD_{50}) of many test substances in laboratory rats.

The incorporation of the test substance into either the drinking water or feeds of the experimental rat may be a justified technique for the oral administration of a substance that the natural route of exposure is either through ingestion as contaminants of food and drinking water; often pollutants of soil, water and food (Plaa, 2004). This technique however will not be so accurate in dosing laboratory rats in other situations because it is not possible to guaranty the fraction of the dose mixed with the food/water that will be ingested because the animal may partially or totally refuse these as a result of unaccustomed taste or flavor.

Another commonly used improvised technique amongst biomedical researchers is the use of the orogastric tube (Agoreyo and Adjene, 2002). However, unpublished remarks about attempts to use the smallest size of plastic orogastric tube (OGT, size 8G) to orally administer test substances to laboratory rats suggest that it is often difficult, traumatic for the animal and unsuccessful. Perhaps the right technique of passing the orogastric tube (OGT) needs to be elucidated and thereafter learnt by researchers and technologists in this part of the world.

Our experience with the use of the Medicut /Mediflon intravenous cannula to administer solutions of test substances to laboratory rats can best be described as successful and encouraging.

Since stumbling at it, we successfully used the technique to orally dose over 50 rats with between 0.7 to 3.5 ml of a uniform stock solution of a plant extract, daily for twenty-eight days. And in this period we accurately delivered in every instance the intended volume, as there were no spillages from either overflow or regurgitation by the animals. We also did not observe death of any of the experimental rat midway into the research work, two frequent complications of the use of the syringe without a cannula. The use of this technique enabled us to easily determine the oral LD_{50} of the plant extract without need to unjustifiably resort to using the parenteral routes as is commonly practiced by biomedical researchers in this part of the world.

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