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QUERY ANSWER REPORT

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Question answered: Can commercial thickeners be added to medication?

Our ref: 128767 Date: 18/09/2015 Pages: 6

BACKGROUND

Addition of commercial "thickening" powders (usually starches or gums) to liquids is a common method of reducing the risk of liquid aspiration and its consequences in patients who have difficulty swallowing. The thickened liquid moves more slowly in the oral cavity, and it is therefore easier for the patient to organise their swallow in order to direct the substance towards the oesophagus and away from the trachea. Liquids are usually thickened to one of three viscosities: "nectar", "honey", and "pudding", with "nectar" being the thinnest and "pudding" the thickest.

A problem arises when the dysphagia patient requires oral medication. Many such patients cannot swallow tablets, but the liquid medications as supplied by the manufacturer are thin enough that aspiration is a possibility.

The question is whether commercial thickening powders can be added to liquid medications or crushed/dispersed tablets in order to facilitate safe administration to patients with swallowing difficulties.

ANSWER

The issues involved fall into several areas:

- Suitability of the drug formulation (e.g. availability of liquid formulation or suitability for crushing/dispersing).
- Effect on drug absorption of administration with *any* other substance (e.g. food).
- Effect on drug absorption of administration with thickening agents (generally starches or gums).
- Effect on drug formulation of adding a thickener.
- Interaction between drug and thickener.
- Effect on the thickened fluid of adding a medication (if medication is to be added to, for example, a thickened beverage).
- Legal and ethical: avoiding covert medication, off-licence administration of a licensed product, and avoidance of the preparation of an unlicensed medicine.

SUITABILITY OF DRUG FORMULATION

The availability and choice of a suitable formulation (e.g. patch/liquid/crush tablets/open capsules) for a patient with swallowing difficulties is beyond the scope of this enquiry.

The following UKMi Medicines Q&As should be consulted:

294.3: *What are the therapeutic options for patients unable to take solid oral dosage forms?*
339.3 Crushing tablets or opening capsules in a care home setting

They are available via NHS Evidence.(1)

ADMINISTRATION OF MEDICINES WITH FOOD SUBSTANCES

It is well known that some medicines should not be administered with food, as to do so either delays absorption or changes the extent of absorption of the drug. Medicines so affected to a clinically relevant extent have a warning in their product literature, stating that they should be taken on an empty stomach or, alternatively, should be taken with food.(2)(3)

Food substances may affect drug absorption in different ways, some of which are relevant to the administration of medication with thickening powders and some of which are not.

Acid stability/dependency

Some drugs require an acid environment for reliable absorption, such as amprenavir, itraconazole and ketoconazole. These drugs require administration with food in order to increase dwell time in the acid environment of the stomach.(3) Administration with thickeners is unlikely to adversely affect such drugs, although if a patient has hitherto been poor at taking their medication with food, increased absorption may result in increased efficacy and/or adverse effects.

On the other hand, drugs which are unstable in an acid environment (e.g. azithromycin, isoniazid, phenoxymethylpenicillin) should be taken on an empty stomach in order to minimise their exposure to stomach acid.(3) Administering such drugs with a thickener, which will increase dwell time in the stomach, risks reducing drug absorption and thus efficacy.

Delayed gastric emptying

Meals slow down gastric emptying.(3) As long as the total amount of drug absorbed is not affected, this is not clinically relevant in most cases. It becomes relevant where a fast onset of action is desired (e.g. when-required analgesics). This should be taken into account when administering medication with food thickeners.

Absorption enhanced by fat or bile acids

The absorption of some lipid-soluble drugs (e.g. isotretinoin) is enhanced by administration with a high-fat meal. It is thought that such drugs become absorbed into the lymphatic system by becoming incorporated into the bile-acid micelles of the fats in the food. In this way losses due to first-pass liver metabolism and gut wall metabolism are minimised, and bioavailability is increased.(3)(4) This is unlikely to be affected by co-administration with food thickeners, as thickeners do not contain fats. Hence, a drug requiring administration with food to take advantage of fat-enhanced absorption should still be administered with a fat-rich meal (or milk, in some cases), even if thickener is used.

Chelation

Some medications, e.g. bisphosphonates, ciprofloxacin, are prone to chelation. This is a problem with substances such as milk, which contain divalent cations (e.g. calcium) and antacids.(4)

MIXING MEDICATIONS WITH FOOD THICKENING PRODUCTS

Manufacturers of thickening products were contacted. Abbott, Nutricia, Sutherland, and Vitaflow had no advice or information to give regarding mixing their product(s) with medication.

Fresenius Kabi, M&A Pharmachem and Nestlé advised as below:

Fresenius Kabi (Thick & Easy)(5) advise:

1. *Always check with a pharmacist or the drug manufacturer that that medication can be mixed with a food starch.*
2. *Mix the Thick & Easy with water to the correct consistency.*
3. *Add the medication in liquid/syrup form or tablets crushed to a fine powder.*
4. *Additional Thick & Easy may be needed if the consistency changes.*
5. *Administer orally as prescribed.*

They also note, helpfully, that the pH of Thick & Easy is 7.2.

M&A Pharmachem(6) advise:

Using Medication with Thicken Aid

Thicken Aid is a modified natural starch based thickener and will be digested in the small intestine, where 98% of the available fluid will be released.

Step 1. Remember to always check with your pharmacist or the drug manufacturer that the medication can be mixed with a food starch.

Step 2. Firstly mix the Thicken Aid with water to the correct consistency, as advised by your Speech and Language Therapist (instructions on how to achieve the different consistencies are printed on the label).

Step 3. Add the medication in liquid/syrup form or crushed tablets to a fine powder or open Capsules and empty the content (crush the content if not fine powder).

Step 4. You may add additional Thicken Aid if needed if the consistency changes

Step 5. Administer orally as prescribed.

Nestlé stated:

Resource ThickenUp Clear can safely be used with medications. The ingredients of ResourceThickenUp Clear are all approved food ingredients consumed on a daily basis.

Resource ThickenUp Clear is regarded as a FSMP (food for special medical purposes) and should in the case of food/drug interactions be treated as a normal food.

Resource ThickenUp Clear will not influence the absorption and efficacy of medication, unless it is contraindicated to take with food.

It is important to note Resource ThickenUp Clear contains 19% soluble fibre, which if introduced to the diet too rapidly could potentially lead to diarrhoea. In this case, a gradual increase is recommended.

Effect of food thickening products on drug dissolution and absorption

As well as slowing gastric emptying (as per meals, above), food thickening products have the potential to delay the dissolution of drugs.(7) As drug absorption depends on dissolution, there is therefore the potential for food thickeners to delay drug absorption beyond their effect on gastric emptying.

Drugs which are absorbed throughout the GI tract are not likely to be significantly affected by a delay in dissolution. However, drugs which have only a narrow absorption window may be carried past their absorption window, thus reducing absorption.

As food thickening products act in some ways like food (particularly the starch-based products), any drug which suffers decreased absorption in the presence of food is likely to have its absorption reduced by thickening products.

Interaction between drugs and thickening products

Food thickening products generally contain either:

- Modified maize starch with or without maltodextrin OR
- Maltodextrin and xanthan gum with or without guar gum

Starch based thickeners cause a liquid to become thicker as the starch molecules swell. Gum based thickeners cause entangled meshes in which water molecules become trapped.(8)

Maltodextrin is a mixture of saccharide polymers. It does not appear to interact with any specific drugs.(9)

Xanthan gum is a high molecular weight polysaccharide gum, and is prepared as the sodium, potassium or calcium salt.

A synergistic reaction occurs between xanthan gum and guar gum, resulting in enhanced viscosity. However, this reaction is inhibited by the presence of salt.(9)

Known interactions with specific drugs

Amitriptyline, tamoxifen and **verapamil** have been found to be incompatible with **xanthan gum**,(10) and therefore it would be preferable not to mix these medications with thickeners containing xanthan gum.

Guar gum has been noted to reduce the peak levels, and reduce the total absorption of **phenoxymethylpenicillin** by approximately a quarter, and also to impair the absorption of some formulations of glibenclamide.(11)

Effects of thickening on drug formulation, and vice versa

There are anecdotal reports(12) of unexpected effects when thickener is added to medication, (or when medication is added to a thickened fluid) particularly with liquid formulations. This may involve:

- The thickener not mixing properly with the drug formulation. Sometimes this problem may be resolved by adding more water.
- The thickener not 'thickening' as expected. Sometimes this problem may be resolved by using a different thickener.

It is therefore wise to check beforehand that a particular thickening product will 'work' with a particular medicine formulation (this applies to different formulations of the same drug, too).

LEGAL IMPLICATIONS

Unlicensed use

Only doctor, dentist, nurse/pharmacist independent prescribers and supplementary prescribers working within a clinical management plan can authorise the administration of an unlicensed product to a patient (Human Medicines Regulations 2012 reg. 167).(13)

Therefore, if a medicine is to be administered outside the terms of the product licence (e.g. by crushing it or by administering it in a way not intended, for example by mixing it with thickener before administration) administration must be authorised by such a prescriber.

Mixing Medications

Mixing more than one drug together, where one is not the vehicle for the other, to be administered as a "cocktail" legally constitutes the manufacture of a new unlicensed medicine (*not* just the off-licence administration of a licensed medicine).(14)

Other than persons holding a manufacturer's licence, only certain groups of healthcare professionals are permitted to mix medicines.

The Human Medicines Regulations 2012 reg. 20 states that doctors and dentists are allowed to mix medicines, and to direct others to do so. Nurse and pharmacist independent prescribers can mix medicines themselves and direct others to mix. Supplementary prescribers can only mix medicines or direct others to do so if this forms part of the clinical management plan for an individual patient.(13)(15)

No other healthcare professionals are permitted to mix medicines (e.g. non-prescribing nurses, or healthcare assistants) unless they do so in accordance with the *written* instructions of a prescriber as above.(13)

A person who contravenes the Human Medicines Regulations by preparing an unlicensed medicine commits a criminal offence and is liable to a fine not exceeding the statutory maximum on summary conviction (in a magistrate's court) or to a fine or imprisonment for a term not exceeding two years, or both, on conviction on indictment (in the Crown Court).(13)

Beyond the legal implications, there are clinical implications. In most cases, the compatibility of such mixtures will be unknown, and the patient is put at risk of unexpected interactions, possibly resulting in unanticipated effects, or therapeutic failure.

Covert Administration

If the medication is administered covertly (i.e., without the patient's knowledge), then the legal and ethical implications of covert administration will apply. These are discussed further in the UKMi Q&A on the covert administration of medicines, which is available via www.evidence.nhs.uk. (16)

SUMMARY

- For further guidance regarding the suitability of medicines to be crushed/dispersed/opened, consult your pharmacist and UKMi Q&As:
    - *294.3: What are the therapeutic options for patients unable to take solid oral dosage forms?*
    - *339.3: Crushing tablets or opening capsules in a care home setting*
- Administering medicines in thickened fluid is usually off-licence. Administration of a medicine off-licence can only be authorised by an independent prescriber (doctor, dentist, pharmacist, nurse) or a supplementary prescriber acting under a clinical management plan.
- Mixing medicines together to administer as a "cocktail" is manufacturing a new medicinal product. This is a criminal offence unless it is done in accordance with the *written* instructions of an independent or supplementary prescriber as above. It may also adversely affect the safety and/or efficacy of any or all of the medicines involved.
- The formulation of medicines should only be altered (e.g. by crushing, dispersing, or mixing with anything that is not included in the manufacturer's instructions) when necessary, and when it is safe to do so. The safety can be checked by consulting a pharmacist.
- Adding thickeners to medication can alter the speed and extent of the absorption of the medicine, and therefore its effects. The patient should therefore be reviewed as necessary to ensure that their drug therapy is still effective.
- Medicines which must be administered on an empty stomach are particularly likely to be adversely affected by mixing with thickeners.
- Sometimes mixing a medicine with a thickener can have unexpected effects on the formulation. It is therefore wise to try it out in advance, before it is necessary to administer it to the patient.

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