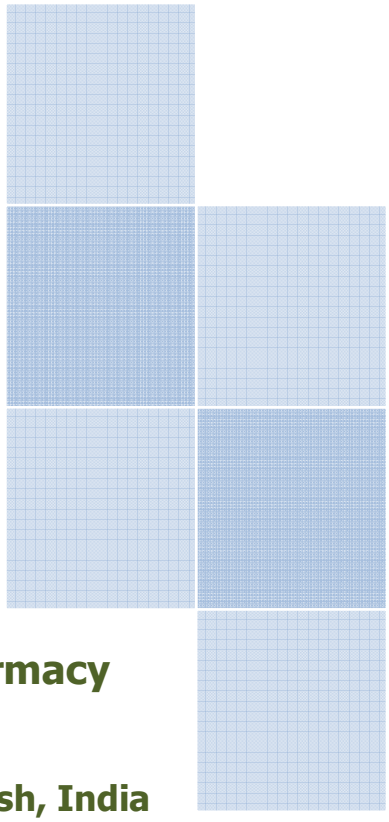
GRCP InfoApex

Half yearly news letter

Issue-4, Apr 2013



Gokaraju Rangaraju College of Pharmacy

Imparts Pharmaceutical Education of International Standards

Bachupally, Hyderabad-90. Andhrapradesh, India

Contents

Motto of this Journal
1. To provide scientific, technical and social welfare updates
2. To promote scientific drafting among staff and students
3. To circulate institutional updates
4. To build flat form to serve the community
5. To identify and appreciate potential achievements

BIO-RELEVANT DISSOLUTION MEDIA

Mr. Panikumar. D. Anumolu, M. Pharm

Dissolution testing plays many key roles in the development and production of solid dosage forms. At the early stage of the drug research and development, dissolution testing is used for API characterization and formulation screening. It is also employed to develop and evaluate the performance of new formulations by examining drug release from dosage forms, evaluating the stability of these formulations, monitoring and assessing the formulation consistency and changes.

For the release of drug products, dissolution testing serves as an important QC tool which is used to verify manufacturing and product consistency. The design of dissolution testing used for QC is primarily based upon the selection of discriminatory media, apparatus, and conditions that can be used routinely for QC purposes. Nevertheless, there is an increasing demand for the development of biorelevant dissolution methods that can provide some predictive estimates of the drug release with respect to the *in vivo* drug product performance.

Limitations of conventional dissolution media:

- Not surrogate the GI environment.
- Not possible to forecast the in-vivo performance.
- Over discriminative.
- Non-discriminative

Bio-relevant dissolution testing

Dissolution process is considered as an important *in vitro* tool for evaluating the bioequivalence of products. Such a method, if properly mimic the *in vivo* conditions, it would surrogate the *in vivo* studies. The biopharmaceutical classification system classifies the drugs into four basic groups according to their solubility and permeability properties. Bioequivalence problems arise in class-II and class-IV categories of Biopharmaceutical Classification of Drugs (BCS). In fact, dissolution is a solubility related phenomena. *In vitro* media is formulated as bio-relevant media, which should be able to mimics the *in-vivo* environment. *In vitro* dissolution media is made biorelevant by including varying levels of bile salts, lecithin and fatty acids

Oral administration is the most convenient way to deliver drugs, and therefore the most preferred. However, the oral route is very complex based on the physiological conditions encountered by the drug as it passes from the mouth to the absorptive sites in the intestine. When moving from the stomach through the pylorus into the small intestine, the drug will meet a rapidly changing environment including bile and pancreatic secretions which will introduce different enzymes and surface active bile components, and increase in pH from acidic to neutral.

Physiological factors such as the rate of gastric emptying, intestinal motility, blood flow, as well as volume, composition and pH of alimentary secretions are known to impact the rate and/or extent of drug absorption. The basic parameters determining the absorption of a drug compound after oral administration are its solubility and permeability in the conditions associated with the gastro-intestinal (GI) tract. For these reasons, considerable research effort has focused on developing in vitro GI fluids that mimic in vivo conditions.

Unlike dissolution methods used for QC in which their design is primarily based upon drug substance physicochemical properties and formulation principles, biorelevant dissolution methods are designed to closely simulate physiological conditions in the GI tract. However, it should be noted that the physicochemical properties of the drug substance (e.g., solubility) and its formulation

(e.g., immediate or extended release dosage forms) play a key role in selecting an appropriate type of biorelevant dissolution medium (e.g., gastric or intestinal medium), apparatus (e.g., a single vessel or multiple vessels), and test conditions (e.g., agitation speed and duration of test), since these drug substance and formulation characteristics impact the location where the drug dissolution takes place in the GI tract.

Importance of biorelevant media

Simulation of gastrointestinal conditions is essential to adequately predict the *in vivo* behavior of drug formulations. To reduce the size and number of human studies required to identify a drug product with appropriate performance in both the fed and fasted states, it is advantageous to be able to pre-screen formulations *in vitro*. The choice of appropriate media for such *in-vitro* tests is crucial to their ability to correctly forecast the food effect in pharmacokinetic studies[9].

Biorelevant dissolution media for gastric conditions

it is logical to use a dissolution medium that reflects the gastric conditions. The minimum physiological parameters that need to be considered here include pH, surfactants and enzymes. To simulate gastric conditions in the fasted state, the pH values of a gastric dissolution medium should be in the range of 1.5- 2.5. In addition, surfactants, such as SLS, should be added into the medium to lower its surface tension close to the *in vivo* values.

Table 1: Composition of S.G.F media in the fasted state

SGF media without enzyme	
Sodium chloride	*0.6g*
Hydrochloric acid	*2.1g*
Deionized water	*upto 300 ml*

Due to its simplicity this medium can also be used for QC dissolution testing. To simulate the fed state in the stomach, the use of milk and Ensure may be appropriate, since these media offer appropriate ratios of fat to protein and fat to carbohydrate. However these media are not suitable for routine quality control testing due to the difficulties in filtering and separating the drug substance from the medium for analysis.

Bio-relevant dissolution media for intestinal conditions

For poorly soluble drugs (e.g., BCS Class II drugs that are neutral or weak acids), it may be more appropriate to use a dissolution media that mimics the intestinal conditions. The dissolution of drug products in the small intestine is influenced by physiological factors including but not limited to pH, endogenous secretions from the pancreas and gall bladder (e.g., bile salts, lecithin and digestion enzymes) and food effects.

In the small intestine, secretion of bile from the gallbladder in the duodenum leads to high concentration of bile salts and phospholipids (lecithin), resulting in the formation of mixed micelles even in the fasted state. These bile salts and lecithin may have a significant enhancing effect upon the dissolution rate of poorly water soluble drugs by improving wettability of solids and by increasing the solubility of drug substance into mixed micelles. A commonly used medium for simulating fasting conditions in the proximal small intestine is fasted state simulated intestinal fluid (FaSSIF).

Table 2: Composition of Fasted state simulated intestinal fluid (FaSSIF)

FaSSIF (pH 6.5)	
Sodium taurocholate	*3mM*
Lecithin	*0.75mM*
NaH_2PO_4	*3.9g*
KCl	*7.7g*
NaOH	*0.35g*
Deionized water	*up to 1 liter*

This media was based on experimental data in dogs and humans for the concentration of bile components, pH value, buffer capacity and osmolality. The pH value was chosen to be 6.5, which closely resembles the values measured from the mid-duodenum to the proximal ileum. Sodium taurocholate was

often used as a representative bile salt since cholic acid is one of the more common bile salts in human bile. The ratio of phospholipids to bile salts employed in these media is approximately 1:3, which reflects the *in-vivo* ratio that is generally found to be between 1:2 and 1:5. In addition to the fasted state, a dissolution medium simulating intestinal conditions in the fed state should assume a lower pH value, higher buffer capacity and osmolality. Here acetic acid buffer is used instead of the phosphate buffer to achieve higher buffer capacity and osmolality while maintain a lower pH value. Taurocholate and lecithin are present in considerably higher concentrations than those in the fasted state medium.

Table 3: Composition of fed state simulated intestinal fluid (FeSSIF)

FeSSIF (pH 5)	
Sodium taurocholate	*15mM*
Lecithin	*3.75mM*
Acetic acid	*8.65g*
KCl	*15.2g*
NaOH	*4.04g*
Deionized water	*upto 1 liter*

Due to their complex composition, availability of costly surfactants (sodium taurocholate and lecithin), and questionable storage stability, these media are expensive, and their use is limited as a regular quality control medium. But a simple test medium can be developed which work almost like bio-relevant media as well as regular quality control media is the replacement of natural bile components (sodium taurocholate) and lecithin with different type and concentrations of surfactants.

Mr. Panikumar. D. Anumolu, M. Pharm
Sr Asst Professor,
Department of Pharmaceutical Analysis,

NATURAL METHODS TO PREVENT KIDNEY STONES

Ms Radha Gayathri A

Pain due to kidney stone is excruciating and patients usually land up in emergency. In acute stages usually analgesics are prescribed, surgeries are done in some cases. Shock wave therapies can also be given to avoid surgery, so as to break the stone. However all these treatment will cost a lot to patient. One can avoid all these expenses by trying home remedies to prevent kidney stone. Their success rates are also high, if one follows them strictly. You have to adjust your diet to avoid the formation of these mineral deposits comprised of calcium, uric acid or the amino acid cysteine.

Acidic urine is associated with xanthine, cystine, uric acid, and calcium oxalate stones. More alkaline diets help prevent these kind of deposits. Softdrinks, coffee, alcohol, products containing corn syrup and most forms of animal protein have an acidic effect on the body. When stones are composed of calcium, magnesium phosphates, and carbonates, the diet should be so regulated as to maintain acidic urine.For controlling the formation of calcium phosphate stones, the intake of calcium and phosphates should be restricted. Foods which should be avoided are wholewheatflour,chickpea,peas,soyabean,beet ,spinach,cauliflower,turnips,carrots,almonds, and coconuts. In case of uric stones, foods with high purine content such as sweet breads, liver, and kidney should be avoided.

Some fruits and vegetables have more alkaline effect, while others are more acidic. Some otherwise healthful foods such as rhubarb, spinach, beet greens, sorrel, green tea, and chocolate can contribute to kidney stone formation because they contain oxalic acid.

Drinking plenty of pure water also helps discourage the formation of mineral deposits in the kidneys. The patient should take a low protein diet restricting protein to one gram per kilogram of food.

CELERY SEEDS (vammu/vaamu): Can help dissolve stones. Simply boil 2 cups of water and then add 2 tablespoon of celery seeds. Cook till the seeds are soft and then strain the seeds from the water. Drink a ½ cup once every hour. Western herbal remedies to prevent kidney stones include meadowsweet, sarsaparilla, joe-pye weed and plantain which help cleanse excess uric acid from the kidneys.

GOLDENROD: Is used to treat or prevent kidney stones. It has the ability to flush water from the body, along with anti-inflammatory and antimicrobial properties. Add 2-3 teaspoon of dried herb in one cup of hot water and let stand for 10-15 minutes. Strain and drink 3 times daily. Drink plenty of water throughout the day when taking this herb.

KIDNEY BEANS also known as dried French beans or Rajmah are regarded as a very effective home remedy for kidney problems, including kidney stones

Ms. A. Radha Gayathri
M. Pharm II/I,
Department of Pharmaceutical Analysis,

FREE RADICALS AND ANTIOXIDANTS

Ms Spoorthy Paladi, Mr Pani Kumar.D.Anumolu

Free radical is a chemical species with single unpaired electron in the outermost shell, and is capable of independent existence. A free radical is easily formed when a covalent bond between entities is broken and one electron remains with each newly formed atom. Free radicals are highly reactive due to the presence of unpaired electrons.

There are many **causes** for the generation of free radicals in our body such as:

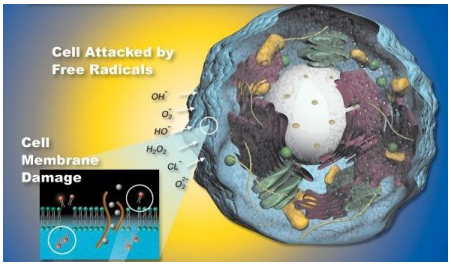
- The ultraviolet light in sunshine - that's why people who spend too much time in the sun are more likely to get skin cancer and cataracts.
- Toxins of all sort such as: tobacco smoke
- The poisonous wastes of our own metabolism
- Man-made toxins like air pollution and pesticides.
- Most commonly from ATP production (electron transport chain)
- During inflammation

The most common free radicals formed in our body are:

1. Superoxide anion (O_2-.)
2. Hydroxyl radical (OH.)
3. Singlet oxygen ($1O_2$)
4. Hydrogen peroxide (H_2O_2)

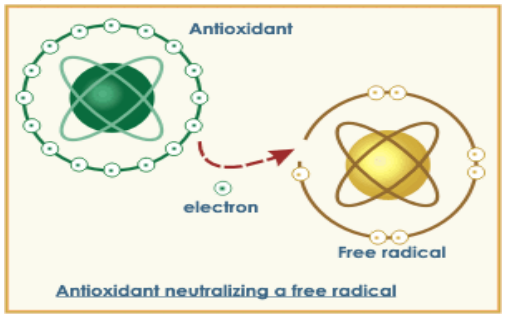
IMPORTANCE OF FREERADICALS: The body's immune system cells purposefully create them to neutralize viruses and bacteria and they help in transferring the energy

EFFECT OF FREE RADICALS: The excessive production of free radicals leads to lipid peroxidation, oxidative modification of proteins, DNA damage, cancer, ageing, cataract, Parkinson's disease etc.



Antioxidants:

Antioxidants are molecules which can safely interact with free radicals and terminate the chain reaction before vital molecules are damaged.



Generally antioxidants work by 2 mechanisms:

- Hydrogen donation to free radicals by antioxidants (AH).
- Formation of a complex between the lipid radical and the antioxidant radical (free
- radical acceptor).

To prevent free radical damage the body has a defense system of *antioxidants.*

They scavenge free-radicals. They are:

- Superoxide dismutase

- Catalase
- Glutathione peroxidase

The main antioxidant foods are:

1. **Carotenoids** – they promote clear vision, prevent premature aging of skin, reduce the risk of cancers, cataracts and blindness.
2. **Vitamin C** with bioflavonoids- it prevents wrinkles, keeps skin and bones healthy, and strengthens the immune system and prevents the oxidation that causes cataracts, arthritis, heart disease and cancer.
3. **Vitamin E** (mixed tocopherols) -it reduce the risks of heart disease, cancer and other age-related degenerative diseases.
4. **Selenium** – a mineral antioxidant- it boosts immunity, reduces anxiety and depression and maintains healthy hair and nails and slows down ageing.

Antioxidant rich food products:

1. **Fruits:** Berries (Cherry, blackberry, strawberry, raspberry, black currant), Pomegranate, Grape, Orange, plum, pineapple, kiwi fruit, grapefruit, guava, tomatoes, papaya.
2. **Vegetables:** Kale, chili pepper, red cabbage, peppers, parsley, artichoke, spinach, lemon, ginger, spinach, broccoli, beets, carrots, sweet potatoes.
3. **Dry Fruits:** Apricots, prunes, dates.
4. **Legumes:** Broad beans, pinto beans, soybeans.
5. **Nuts and seeds:** Pecans, walnuts, hazelnuts, ground nut or peanuts, sunflower seeds, almonds.
6. **Cereals:** Barley, millet, oats, corn.
7. **Spices:** Cloves, cinnamon, oregano
8. **Selenium Sources** are healthy high protein foods like seafood, eggs and meat, whole wheat, brown rice and other whole grains.

Mr. Panikumar. D. Anumolu, M. Pharm
Sr Asst Professor,

Ms. Spoorthi P
M. Pharm II/I,
Department of Pharmaceutical Analysis,