The primary objective of programs and techniques for studying the stability of emulsions is to predict the shelf life of these emulsions at normal storage conditions. Since emulsions are thermodynamically unstable, the formulation of emulsions with good storage stability is a difficult, time-consuming task. The formulator attempts to make some estimate of the product's required shelf life. This time normally includes storage by the manufacturer after production, shipping time, storage by the vendor, and the time required until the product is used up by the ultimate consumer.

A shelf life of no less than two and no more than five years is the currently accepted expectation for most consumer products. To lessen the time expended many types of stress tests are used to provide a basis for prediction of stability, and data from such tests is useful but must be treated with caution regarding its relevance to the use situation and/or actual long-term stability. It is the formulator's responsibility to select the stress conditions and test methodologies which will be used for shelf life prediction. Such a shelf life prediction should coincide with the shelf life demands established on the basis of estimated storage and use-up times. It is important to emphasize that abuse of an emulsion is useless for predicting stability under normal storage and use conditions. It is important, therefore, to select storage and stress conditions with utmost care. The formulator is then faced with the problem of assessing, by one or more test methodologies, how seriously the emulsion has been has been damaged by the stress conditions. If critical damage has occurred even under sensible stress conditions, the stability of the new emulsion is comparable to that of a similar commercially distributed product exhibiting an adequate shelf life.

The most practical approach is to rely on a comparison between the “new” product and a similar “old” product that has shown acceptable real life stability. Stability testing programs are not absolute: acceptance, i.e., the judgment that a product has adequate stability, is a compromise between market acceptance and expected instability. Comparison to an established stable product is the only sensible yardstick for predicting the shelf life of a previously untested preparation. Any testing recommended should, whenever appropriate, be conducted in tandem with similar tests on an established preparation.

**INSTABILITY OF EMULSIONS**

Physical instability of disperse systems in general, and of emulsions in particular, is caused by a physical phase separation of some type, which leads to changes in appearance, consistency, redispersibility and performance. By their multiphase nature, emulsions are more complex than suspensions because of the ability of the surfactant to diffuse in and out of the emulsion dispersed and continuous phases and because of the potential mobility of the surface layer itself. As soon as an emulsion is prepared, time and temperature-dependent processes begin to try to effect separation. During storage the progressive changes in an emulsion's instability proceeds through stages of creaming,
reversible aggregation or floc-
culation towards irreversible
aggregation (coalescence).

Greatest initial concern is
gravitation separation, which is
manifested in an emulsion
either by creaming or sedimen-
tation. Under the influence of
gravity, suspended particles or
droplets tend to rise or sedi-
ment, depending on differ-
ences in specific gravities
between the phases. Hence, if
creaming takes place without
any aggregation, the emulsion
can be reconstituted by shak-
ing or mixing. If an emulsion
creams up (rises) or creams
down (sediments), it may still
be pharmaceutically acceptable
so long as it can be reconstitu-
ed by modest shaking. Similar
considerations apply to cos-
metic emulsion: though in
cosmetics creaming usually is
unacceptable because any
unsightly separation makes the
product cosmetically inelegant.
Creaming or sedimentation
will bring particles of the in-
ternal phase into very close con-
tact, producing several sec-
ondary phenomena. First of
these is flocculation, which
may take place before, during,
or after creaming. Flocculation
is best defined as the associa-
tion of particles within an
emulsion or suspension to form
large aggregates which can eas-
ily be dispersed upon shaking
and which show no evidence
of coalescence. In fact, in some
suspensions and emulsions
floculation is a desirable char-
acteristic because simple shak-
ing is not considered a serious
detriment to product mar-
ketability.  

At any level of phase vol-
ume ratio discrete droplets are
in a state of flocculation which
is responsible for the rheologi-
cal properties of the emulsion,
giving it a higher apparent vis-
cosity than would occur with
completely separated particles.
It is this flocculation, and the
level of rheological structure
produced, that also gives emu-
sions their desirable character-
istics as drugs and cosmetics
and which assists in resisting
instability. In contrast to flocc-
culation, if the internal phase
coalesces to form larger parti-
cles (not aggregates), signifi-
cant non-uniformity may
result, and if coalescence con-
tinues, large droplets or crystal-
lites will be formed which are
unsightly and unacceptable to
the consumer. Hence, any evi-
dence for formation of larger
droplets by merger of smaller
droplets suggests that the
emulsion eventually will sepa-
rate completely.

Major factor preventing
coalescence in floccu-
lated and unfloccu-
ed emulsions is mechanical
strength of the interfacial bar-
rier. This is especially true in
o/w systems containing non-
ionic surfactants and in w/o
emulsion systems in which
electrical effects are negligible.
Coalescence can be avoided by
the formation of a thick inter-
facial film from macromole-
cules or from particulate solids.
This is the reason a variety of
natural gums and proteins are
so useful as auxiliary emulsifi-
cers when used at low levels,
and can even be used as prima-
ry emulsifiers at higher con-
centrations. Higher bulk vis-
cosity occurs because of excess
polymer and surfactant dis-
solved in the external phase.

In the case of concentrated
surfactant and polymer solu-
tions, prevention of particle
interaction also may be
achieved by formation of liquid
 crystals. Liquid crystals
impurt orientational ordering
in the phases, this being ade-
quate to provide for increased
viscosity, but not strong
enough to prevent flow.
Hence, liquid crystals can be
considered visous liquids and
exhibit dualism of physical
structure. They stabilize an
emulsion by two mechanisms:
1) they form a barrier around
the emulsion droplets and
strengthen the o/w interface,
thus reducing the likelihood of
coalescence; and 2) they form
a "gel network" extending from
the surface of the emulsion
droplet movement, thus
inhibiting coalescence.

Instability of emulsions can
also result from chemical insta-
bility (especially hydrolysis of
surfactants), microbial destruc-
tion of a critical emulsion
component, or photochemical
processes. In this review it is
assumed that the formulator
has combined only stable
ingredients, has created a pro-
perly preserved product, and has
protected his preparation
against photochemical decom-
position. Chemical instability
of emulsion ingredients should
be anticipated by the formula-
tor. If such instability is
observed during long-term sta-

STABILITY TESTING

General objective of a sta-
Stability testing of emulsions

PART I

Stability testing of emulsions is to determine whether a given product in the container in which it is to be marketed has adequate shelf life under the conditions of the market in which it is to be sold. It embraces not only the chemical and physical stability of the product but also possible interactions between the product and container which may adversely affect either or both. Unfortunately, no firm rules have been provided to the formulator for predicting stability, leaving laboratories to their own devices to interpret data. Suitable stress tests still are used relatively seldom by manufacturers of emulsions though their reproducibility often has been demonstrated reliably. In many instances storage stability is judged solely on the basis of a visual macroscopic assessment of the appearance of the emulsion. This can afford considerable information. Visual inspection, sometimes with the aid of a magnifying lens or special lighting, provides formulators with an obvious method for the detection of separation or instability. The observations and the recording of data obtained during visual inspection are highly subjective, and unexplained differences between observers (or laboratories) have not been resolved. Nevertheless, observations of rising or settling and similar phenomena should be made routinely during stability studies.

While visual testing of emulsions usually corresponds to the assessment made by the customer, without doubt, emulsions separated into two or more layers can be considered unstable. However, whether the reversible creaming often observed with cosmetic emulsions renders a product usable depends on the tester's subjective judgment. So far no generally valid standards exist for visual assessment of emulsion instability though some authors have tried to introduce a qualitative system to achieve this. A cooperative study among German cosmetic manufacturers attempted to numerically rate visually observed instability phenomena: emulsions showing no signs of instability being given a maximum rating of 9; completely coalesced emulsions receiving a 0, and gradations of 3 and 6 indicating degrees of water/oil separation.

STRESS CONDITIONS

Stress conditions normally employed for evaluating emulsion stability include 1) aging and temperature, 2) centrifugation, and 3) agitation. These methods all can provide valuable information, but one must understand that the greater the degree of acceleration a test attempts to achieve (i.e., the further removed are test conditions from actual market conditions) the greater the risk of changes that never occur under market conditions (i.e., the test no longer merely accelerates changes occurring under "normal" conditions). We have the additional concern of being sure that the accelerated conditions do not introduce new and unanticipated mechanisms of instability, especially those bearing little relationship to what happens long-term.

However, pre-market storage tests for the entire anticipated shelf life of the product (about two to three years) are impractical and emulsions are subjected to accelerated stability testing in a quest to predict shelf life. It is essential to use sound judgment and great care in setting up a meaningful stability program for a given emulsion. If our judgment is reasonably correct we would hope that the stresses applied to accelerate stability allow us to then extrapolate our results to normal storage/use conditions for predicting long-term stability.

Part II of this article will appear in the next issue of DCI.

REFERENCES


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